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FOREWORD

The Department of Surgery of The Johns Hopkins University and Hospital takes pleasure in sponsoring this issue of *The American Surgeon*. The papers were collected by Dr. James Cantrell, and he has very kindly invited me to write this foreword.

Our department consists of General Surgery including thoracic, cardiovascular and pediatric surgery, and the following six divisions (each under the direction of a full-time man): Anesthesiology (Dr. Donald W. Benson), Neurosurgery (Dr. A. Earl Walker), Orthopedics (Dr. Robert A. Robinson), Otolaryngology (Dr. John E. Bordley), Plastic Surgery (Dr. Milton T. Edgerton), and Urology (Dr. W. W. Scott). Each division has its own resident staff and laboratories. There is a small full-time group in each department and a much larger part-time staff. There is a close working relationship with the Baltimore City Hospitals (Dr. Mark M. Ravitch), the Sinai Hospital (Dr. Arnold M. Seligman), and the Veterans Administration Hospital for chest diseases (Dr. Richard F. Kieffer, Jr.).

Most of the papers in this issue are clinical in nature. Some deal with subjects of interest in general surgery; others are concerned with problems in the surgical specialties.

ALFRED BLALOCK, M.D.

THE HEROIC TREATMENT OF ACUTE HEAD INJURIES: A CRITICAL ANALYSIS OF THE RESULTS*

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In recent years a number of procedures, which have much to recommend them, have been advocated to treat more effectively the patient with a severe head injury. That they have aided in accomplishing the desired goal, namely to restore the victim to a normal life, has, at times, been questioned. In an attempt to assess the value of these heroic measures, a series of severely injured patients has been analyzed to determine the degree of rehabilitation of the patient.

The techniques investigated include tracheostomy, hypothermia and lobectomy. A decade ago emphasis was laid upon the relief of uncal herniation by section of the tentorium, but in the last 5 years in this hospital this procedure has been replaced by temporal lobectomy, hypothermia or the administration of intravenous urea. Accordingly no further mention of tentorial section will be made.

MATERIALS AND METHODS

The patients in this series were admitted to the neurosurgical service of the Johns Hopkins Hospital. It is the practice at this institution to see and evaluate all patients with head injuries in the emergency room. Patients with mild cerebral trauma (so-called "concussions") and minor scalp lacerations are observed for 2 to 6 hours and discharged to return for check-up or removal of sutures in 1 to 5 days. The patients with more severe brain damage are observed in an overnight ward and discharged if doing satisfactorily in 24 to 36 hours. Only those patients requiring major craniotomies or debridements are admitted to the hospital on the neurosurgical service. Hence less than 10 per cent of the patients with head injuries seen in the emergency room enter the neurosurgical service. Of those patients admitted in the past 5 years, all requiring lobectomies, tracheostomies, hypothermia, or who succumbed to their injuries are included in this survey of the heroic treatment of head injuries. Thus table 1 gives a tabulation of cases.

There is no doubt that only the most severely wounded patients were subjected to the heroic measures, so that a comparison of morbidity or mortality in patients treated by standard and heroic methods is not valid.

In addition some 13 patients with head injuries treated by hypothermia on the neurosurgical service of Dr. J. D. McQueen at the Baltimore City Hospitals are included.

The surviving patients with one exception have been interviewed and examined from 6 months to 5 years after their injury by one or both of the authors. One patient could not be traced after his discharge from the hospital, and two patients were followed for only about 6 months.

The surgical procedures on the head were carried out under general anesthesia in most cases, as soon as the patient's condition warranted major surgery, usually within 2 to 6 hours after injury.

Tracheostomy. The tracheostomy was usually made under local anesthesia in the conventional manner, and a tube was inserted in the trachea and fastened in place. Moist air was supplied constantly to the tracheostomy tube and oxygen given as required. While a tracheostomy tube was in place a nurse was in constant attendance upon the patient. The tube was plugged when the patient seemed to have no respiratory troubles and, when the corking was well tolerated, the tube was removed, usually 2 to 4 weeks after insertion.

Hypothermia. The degree and duration of hypothermia varied considerably. The cooling was induced by a blanket through which flowed water at any temperature desired. Usually cooling to 90°F. could be obtained within ½ to 2 hours and was usually induced after the patient returned from the operating room where exploratory or definitive surgery was carried out. In some cases the hypothermia was induced before the surgical

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TABLE 1

Types of head injuries treated by standard and heroic measures

Type of Injury	Standard*		Heroic	
	Alive	Dead	Alive	Dead
Skull fractures				
Depressed	28		†	
Compound	13			
Basal	2			
Hemorrhages				
Subdural	27	6	2	8
Epidural	2	1	2	0
Intracerebral				3
Cerebral				
Contusions			1	12
Lacerations		1	6	2
Edema		1	2	3
Others and unknown	3	7	8	4
Total	75	16	31	32

* Standard measures include debridement, evacuation of hematomas, and conservative supportive measures to reduce brain edema such as limitation of fluids, intravenous urea, etc.

† Fractures were associated with most of the cerebral injuries but because the latter were the more serious the cases are listed under that category.

procedure. Temperatures were recorded at least every 30 minutes during hypothermia by a rectal thermocouple. The duration of hypothermia varied from about an hour in one patient who died to 8 days with an average of 4.0 days.

The temperature varied in each case over several degrees, but the lowest reading in any case was 86°F. In table 2 the upper range of temperature for the period of hypothermia is given. The lower range was usually about 4° colder. One patient who seemed to be developing a hyperthermia was maintained at 98 to 99°F. for 3 days, and then allowed to regulate his own temperature; he made a recovery.

Lobectomy. In cases in which a localized laceration of the brain with pulping of nervous tissue had occurred, the macerated tissue was removed. In several cases this consisted of a frontal or temporal lobectomy. In a few patients with marked cerebral edema, the tip of the right temporal lobe was removed to allow a decompression. When the temporal lobe was removed,

TABLE 2

Upper range of temperature during hypothermia

	Temperature (°F.)				
	91	92	93	94	95
Number of cases	12	4	4	7	3

the medial temporal structures were excised and an uncal herniation, if present, relieved.

FINDINGS

If one surveys the mortality of the patients subjected to these heroic techniques (table 3), it is apparent that the death rate is over 50 per cent. One important factor in this mortality is the age, for those patients surviving tracheostomy averaged 20 years younger than those succumbing, in fact the mortality for people over 40 years of age approximated 70 per cent, whereas in patients under 40 years it was about one-half of that. In patients surviving hypothermia, the mean age was 10 years younger than those succumbing (table 4). It seems obvious, then, that young patients are the best candidates for tracheostomy and hypothermia. The number of lobectomized is so small that an analysis is not very valuable.

A mortality of 50 per cent, although formidable, would be permissible if the survivors were in excellent condition. However, as seen in table 5, approximately half of the surviving patients are seriously handicapped; 1 is in a comatose state and has been for months; 2 others vegetated for a year before their death; and 4 have such serious disabilities that they can take care of themselves only with difficulty. If we analyze the group of apparently normal individuals we note

TABLE 3

End results

Technique	Alive	Dead
Tracheostomy	16	20
Hypothermia	11	21
Lobectomy	6	10
Totals.*	25	41

* Some patients had more than one procedure so that the totals are less than the sum of the procedures.

TABLE 4

Age and survival

Technique	Mean Age in Years	
	Alive	Dead
Tracheostomy	26	46
Hypothermia	28	38

TABLE 5

*Status of survivors**

Neurologic State	Tracheostomy	Hypothermia	Lobectomy	Any Procedure
Normal	9†	9	4	13
Residual				
Slight	2	1	1	6
Severe	3	1	1	4
Coma	1	0	0	1
Work status				
At work or regular school	4	5	2	9
Not attending	11‡	6	4	15
Convulsions				
None	10	10	4	17
Temporary	2	1	1	4
Continuing	3	0	1	3

* One not followed up.

† Two patients with marked mental impairment.

‡ Three are attending special school.

the following: Only 4 of the 13 are under 20 and the ages of the others range to 53 years. Of the 9 adults without neurologic disability, 4 are unable to work because of their mental state; 3 patients had depressed skull fractures, and 2 of these might have recovered without heroic measures. Two patients, both children, had subdural collections of fluid and were stuporous on admission. Hypothermia may have helped these cases. One patient suffering from a closed head injury, had his tracheostomy done 11 days after his injury because of respiratory difficulties, otherwise he appeared to be recovering. Another patient suffering from self-inflicted gunshot wounds of the orbit was conscious at the time of admission; his tracheostomy was, in part, indicated by reason of his broken jaw. It would seem, then, that for some patients at least the heroic measures may have been life-saving.

It would appear that 9 of 66 patients treated by these measures were salvaged for relatively normal lives. On the other hand, some 15 patients have such serious neurologic deficit that they are unable to take care of themselves. In the older people, the results of this form of treatment have not been impressive; only 2 of 24 patients over 50 years of age survived in this series. This older group might do better if a more determined effort were made to relieve their condition by less radical procedures.

Experimental studies have shown that cerebral reactions to trauma are markedly delayed or decreased by hypothermia. If such an effect is present in man, one might expect that the brains of people dying of head injuries, who have been cooled, would have less edema and fewer brain stem lesions than untreated victims. By the courtesy of Dr. Richard Lindenberg of the Office of the Medical Examiner of the City of Baltimore, one of us (A. E. W.) was able to review the brains in a series of 40 patients dying of head injuries, 19 of whom were treated by hypothermia. In 16 cases (10 untreated and 6 hypothermic) the histologic preparations were available for study. For purposes of comparative analysis, the findings in the cerebrum, brain stem and cerebellum were assessed in terms of contusions and edema.

Contusions (and lacerations) were considered to be present if there was a grossly visible area of hemorrhagic infiltration of brain tissue associated with dissolution or tearing of the tissue. Small petechial hemorrhages were not considered to meet the minimal requirement of a contusion. In practically all cases there was no question as to the presence or absence of contusions for extensive areas of cortex or brain stem were usually involved. Edema was considered present when an area of brain was swollen, the demarcation between gray and white matter indistinct, or the white matter abnormally soft and its volume increased. These gross findings were confirmed in practically all cases by microscopic demonstration of dilated pericellular and perivascular spaces, neuronal disintegration, areas of demyelinization and in some cases evidence of inflammatory reaction in the involved regions.

The brains were examined using these criteria for contusion and edema without the knowledge of the type of therapy employed after injury. When the results were analyzed no significant difference could be seen in the findings in the two

TABLE 6

Comparison of autopsy findings in head injured patients treated by hypothermia and standard methods

Technique	Total	Cerebrum		Brain Stem		Cerebellum	
		Contusion	Edema	Contusion	Edema	Contusion	Edema
Control	21 (10)*	12	11	8	4	2	5
Hypothermia	19 (6)	17	12	7	9	4	4

* The figures in parentheses indicate the number of cases with histologic preparations.

series (table 6). It must be admitted that the time, duration and degree of cooling varied considerably. Possibly a group of patients treated by hypothermia immediately after injury, maintained at 30°C. for 3 to 5 days might be a more ideal test series, and might approximate more nearly the findings in experimental animals. However, such an ideal situation does not present itself in clinical practice. Moreover, it must be admitted that measures employed in the test group were fairly representative of those used in the treatment of head injuries.

DISCUSSION

The introduction of new procedures to alter favorably the course of a patient with a head injury always raises certain questions. Few procedures are simple and completely innocuous or free of side effects. Thus their performance on individuals who already have severely deranged function—such as is present in the patient with a head injury—may inflict a clinical stress. For this reason one might review the advantages and disadvantages of the heroic measures advocated for the treatment of brain injuries.

Tracheostomy. There is no doubt that the maintenance of an adequate pulmonary ventilation is of prime importance in the treatment of a patient with a head injury. The accumulation of carbon dioxide predisposes to marked changes in the cerebral vascular tree and the blood brain barrier so that edema occurs. Even temporary obstruction of the airway will cause intracerebral alterations which may not be corrected for hours. It is natural that tracheostomy which facilitates the removal of secretions from the trachea, simplifies the administration of oxygen and lessens the tidal air that must be moved with each respiratory effort, should be advocated in patients, unconscious from a head injury, who are having respiratory difficulties due to the accumulation of mucus in the throat or the falling of the tongue into the nasopharynx.

However, tracheostomy is not without complications. Davis and his associates[3] found that major complications such as hemorrhage, pneumothorax, mediastinal emphysema and apnea occurred in about 9 per cent of elective procedures. Lewin[4] reports that in 100 tracheostomies on patients with head injuries 8 per cent had major complications. The seriousness of such accidents in patients with severe head injury cannot be minimized.

It seems wise, therefore, to utilize conservative methods for maintaining a good airway, if possible. Good nursing, postural drainage and suction will be sufficient to maintain pulmonary ventilation in most patients. Only if these simple methods have failed or are inappropriate, such as in the case of a broken jaw or bleeding from nasopharyngeal tissues, need a tracheostomy be performed. We would agree with Lewin,[4] who states, "In severe head injury, tracheostomy is not needed as a routine procedure merely because a patient remains unconscious. An early tracheostomy is indicated for those patients who remain in coma and in whom respiratory exchange is inadequate or respiratory incidents are beginning to appear."

Hypothermia. The advantages of a lowered temperature in decreasing cerebral metabolism, oxygen requirements, reducing reactive edema and lowering the volume of the brain tissue have been well substantiated in both experimental animals and man. However, the cardiac complications, peripheral neuropathies and possible masking of signs of intracranial bleeding are formidable disadvantages. Fortunately, such complications do seem to have occurred rarely in the series of patients with head injuries reported to date. Sedzimir,[5] who treated 30 severely head injured patients with hypothermia (from 30 to 34°C.)

considers it of great value. Lazorthes and Campan[3] believe that moderate refrigeration quickly induced in the first few hours after injury will give best results. However, in their series of 47 patients 13 survived, and only 9 of these were without residuals. It is perhaps noteworthy that in 2 of their fatal cases, only cerebral edema with temporal herniations was found. Wertheimer and Descotes[6] in their series of 36 patients subjected to hypothermia had 21 deaths. They note that patients cooled to temperatures between 27 and 33°C. had a mortality of over 80 per cent (15 of 18) which they suggest might be attributed in part to the effect of hypothermia.

Lobectomy. The removal of all necrotic, hemorrhagic and edematous brain tissue long has been one of the principles of debridement of open head wounds. In closed head injuries this practice has only sporadically been advocated. Yet reports, especially that of Botterell,[1] have indicated that it is highly desirable in some cases. In this hospital, such tissue has been excised, if present, in the course of an exploration for subdural or extradural hemorrhage, or if a tentorial herniation, compromising the brain stem, has resulted from contusion of the temporal lobe. Theoretically this should serve as an internal decompression as well as to remove necrotic brain which might be causing a severe edema.

In discussing the results of the present series of cases, it must be admitted that, although all patients had sustained serious head wounds, not all were moribund. Moreover, it would seem that some procedures were of a prophylactic nature. Such a policy seems justified for, as many have argued, if one waits until respiratory difficulties are too distressing, a tracheostomy may not achieve the desired result that an earlier one would have gained. But this places upon the individual judgment, possibly biased by many considerations, some not medical, the decision as to whether or not a tracheostomy should be done, and at what time. A similar situation exists with respect to the other radical methods of treatment.

Although our observations do not warrant firm conclusions regarding the heroic treatments, they indicate that such measures are not the solution to the problems of head injuries at any period of life and suggest that in the older age groups they may add to the risk of the condition more than they contribute to its alleviation. We would agree with Lewin,[4] who writes, "We have not been impressed with the practical recoveries of older people from head injuries with tracheostomy and in some instances the operation has served only to prolong an illness distressing for relatives and without hope of recovery."

In view of our experiences it would seem that the heroic procedures should be reserved for younger individuals unless some specific indication demands their use in older people. Probably increased emphasis on nursing care, supportive therapy, the administration of urea to control cerebral edema and oxygen therapy would offer more to people with severe head injuries over 50 years of age than vigorous surgical action.

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REFERENCES

1. Botterell, E. H.: On brain injury. Presidential Address, Canadian Neurological Society, Toronto, June 12, 1958.
2. Davis, H. S., Kretchmer, H. E., and Bryce-Smith, R.: Advantages and complications of tracheotomy. J. A. M. A., *153:* 1156, 1953
3. Lazorthes, G., and Campan, L.: Hypothermia in the treatment of craniocerebral traumatism. J. Neurosurg., *15:* 162, 1958.
4. Lewin, W.: Tracheostomy in head injuries. Proc. Roy. Soc. Med., *52:* 409, 1959.
5. Sedzimir, C. B.: Therapeutic hypothermia in cases of head injury. J. Neurosurg., *16:* 407, 1959.
6. Wertheimer, P., and Descotes, J.: L'hypothermie dans les traumatismes cranio-cérébraux. 1st Internat. Cong. Neurol. Surg. 1957, Excerpta Medica 1957: 21.

RETROGRADE PERFUSION OF THE CORONARY SINUS WITH GASEOUS OXYGEN*

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Retrograde perfusion of oxygenated blood into the coronary sinus has been shown to be effective in maintaining the heartbeat in the experimental animal and has been employed to support the human heart in open surgical procedures on the aortic valve. Although reversal of flow through the myocardial vascular bed is distinctly inferior to the oxygenation provided by the normal pathway, protection of the heart from anoxia and its sequellae has been demonstrated for short periods of time. In previous studies on this problem, blood has been used as the perfusate. Within the past several years several groups of investigators have shown that tissues and organs may be maintained in a viable and functional state for prolonged periods by the perfusion of *gaseous* oxygen into the arterial system. The present communication concerns an experimental study of the effect of retrograde perfusion of gaseous oxygen into the coronary sinus on the maintenance of the heartbeat.

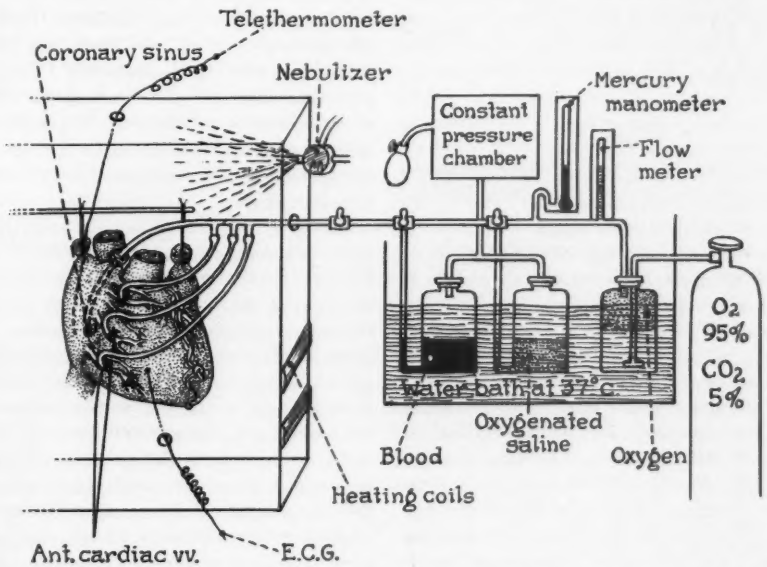

FIG. 1. Diagrammatic illustration of method employed for retrograde perfusion of the heart. A cannula is placed through the right atrial appendage into the coronary sinus and additional cannulae are inserted into the anterior cardiac veins of the right ventricle.

METHODS AND RESULTS

Ten adult mongrel dogs were used in the study. The animals were lightly anesthetized with sodium Pentothal and respiration was maintained through an endotracheal tube attached to a respirator supplied with oxygen. The chest was

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† Investigator, Howard Hughes Medical Institute.

TABLE 1

Retrograde perfusion of the coronary sinus with gaseous oxygen

No.	Heart Weight	Duration	Final State	C.S.*	C.S. + AV†
	gm.	*hr.*			
1	62	3¼	Asystole	+	
2	84	4	Asystole	+	
3	100	4	Asystole	+	
4	96	2	Vent. fib.‡	+	
5	84	3⅔	Asystole	+	
6	60	3¼	Asystole	+	
7	104	3½	Asystole	+	
8	90	6	Asystole		+
9	151	7	Asystole		+
10	117	3⅚	Vent. fib.		+

* C.S., coronary sinus perfusion.

† C.S. + AV, coronary sinus and anterior cardiac vein perfusion.

‡ Ventricular fibrillation.

TABLE 2

Changes in heart rate during retrograde perfusion of the coronary sinus with gaseous oxygen

No.	Time (Hours)								
	Control*	½	1	2	3	4	5	6	7
1	84	14	11	17					
2	44		37	38	40				
3	100	65	22	15	30				
4	100	18	14						
5	83	24	28	75					
6	97	100	33	11					
7	52	60	48	38	53				
8	40	28	33	60	43	28	13		
9	100	47	72	22	36				
10	107	26	24	25	23				
Avg.	81	42	32	33	37				

* Rate of isolated heartbeat while perfused with oxygenated blood before perfusion with gaseous oxygen-carbon dioxide.

entered through the left 4th intercostal space and the pericardium opened. The great vessels were quickly divided, and the heart was removed from the chest. A polyvinyl cannula with a flanged tip was passed through the right atrial appendage into the orifice of the coronary sinus and held in place by a suture ligature. In 3 animals (nos. 8, 9 and 11) several of the larger anterior cardiac veins were also cannulated with small polyethylene catheters. The heart continued to beat during the brief period required to perform the cannulation and then was placed in a transparent Plexiglas unit maintained at 37°C. High humidity was supplied by a constant saline vaporizer. The cannulae in the coronary sinus and anterior cardiac veins were then connected to a reservoir containing oxygenated blood obtained from a donor and kept at 37°C. Retrograde perfusion of the heart at a pressure of 100 mm. Hg was begun. After a strong beat had been restored (usually requiring 2 or 3 min. of blood perfusion) the perfusate was changed to normal saline. All of the blood was washed from the coronary vessels, and perfusion was begun with a humidified mixture of gaseous oxygen (95 per cent) and carbon dioxide (5 per cent) at a rate of 700 to 1500 cc. per min. and a pressure of 20 to 50 mm. Hg. The heart action was monitored constantly by direct observation through the transparent Plexiglas chamber and by an electrocardiographic tracing from a left ventricular electrode. A diagrammatic illustration of the experiment as performed is shown in figure 1.

In the 7 hearts in which the coronary sinus alone was perfused, the heart continued to beat for periods of 2 to 4 hr. (table 1). The average duration of the beat in this group was 3½ hr. Gregg and associates[6] have emphasized the importance of the anterior cardiac veins in the drainage of the right ventricle and when these vessels were perfused in addition to the coronary sinus, the heartbeat continued for an average of 5½ hr. (table 1). In most of the preparations the heartbeat remained obvious for the first 2 hr. and then became gradually weaker and finally barely discernible. Electrocardiographic activity continued until asystole or ventricular fibrillation occurred. The heart rate usually became slower with the passage of time. These data are presented in table 2. An electrocardiogram illustrating the pattern and rate change is shown in figure 2.

DISCUSSION

The concept that the rhythmic contraction of the heart may be maintained by retrograde perfusion of blood through the coronary sinus was first advanced by Pratt[8] in 1897. He reported the observation that the freshly extirpated heart of the cat continued to beat for 1½ hr. when the coronary sinus was perfused with defibrinated arterial blood from a buret with a column only

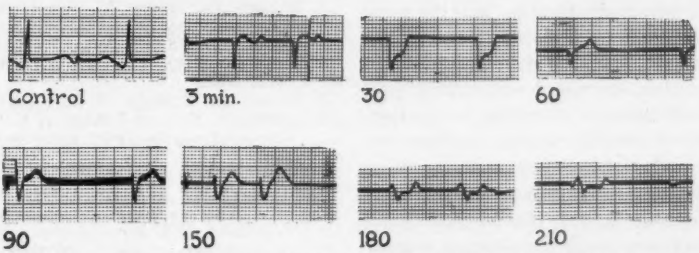

FIG. 2. Electrocardiogram recorded from heart no. 7 with exploring electrode inserted into the interventricular septum with the remote electrode on the left atrial appendage. Paper speed 25 mm. per sec. and amplitude 1 mv. per mm. Tracings are shown during the control period with perfusion of arterial blood and during oxygen-carbon dioxide perfusion at 3, 30, 60, 90, 150, 180 and 210 minutes.

12 cm. in height. Little interest was shown in these observations until 1943 when Roberts[9] made the suggestion that an arteriovenous fistula constructed between the coronary sinus and the aorta might improve the coronary circulation in patients with myocardial ischemia. This procedure was then employed on a number of animals by Beck and associates[1] and was shown to provide protection against induced experimental myocardial infarction. These studies led Beck to the conclusion that retrograde flow through the capillary bed did occur and that arterial blood entering the coronary sinus from the aorta transversed the capillary bed where it gave up its oxygen and emerged into the coronary artery as reduced venous blood. Although the procedure was employed in a number of patients, it subsequently has been abandoned due in part to the high mortality.

In 1956 Blanco and associates[2] employed acute retroperfusion of the coronary sinus in order to provide the myocardium with oxygen during a direct experimental approach to the aortic valve. Gott and associates[5] later demonstrated that retrograde perfusion of oxygenated blood into the coronary sinus of the dog permitted direct-vision procedures on the open ascending aorta and aortic valve for periods up to 20 min. with survival. Nine dogs were used as controls and in these animals the entire body (except the heart) was perfused for 15 min. on cardiopulmonary bypass. In 8 of these animals death occurred and was ascribed to myocardial infarction. These and other studies suggest that although retrograde perfusion may offer protection to the myocardium, there is little question that retrograde perfusion is considerably less effective than arterial perfusion.

In 1902 Magnus[7] showed that the beat of the cat heart could be maintained for an hour with perfusion of gaseous oxygen. Others have shown that tissues and organs may remain in a living and functional state for prolonged periods when the arterial circulation is perfused with gaseous oxygen. This observation was reported first by Bunzl and his co-workers[3] in 1954 when they demonstrated that the spinal cord of the decerebrate frog could be maintained in a reflexly active state for periods up to 24 hr. when the vascular system was perfused with a gaseous mixture of oxygen and carbon dioxide. In 1958 further studies on this problem were reported by Burns and co-workers.[4] They demonstrated that muscular contraction in the perfused, isolated hind limb preparation of the cat could be maintained in a physiologic state for a period of 3 to 4 hr. by perfusion of the femoral artery with gaseous oxygen. These observers also showed that the isolated rabbit heart continued to beat for periods of more than 3 hr. when the coronary circulation was perfused with gaseous oxygen.

In recent studies in our laboratory it has been demonstrated that the isolated heart of the dog will continue to beat for periods up to 8 hr. when the coronary circulation is perfused with gaseous oxygen.[10] In control observations it was shown that the average duration of the heartbeat without perfusion was 18 min. In some of the preparations with oxygen perfusion the electrocardiographic activity continued after cessation of visible contraction and was observed for periods up to 4 hr. after the last visible beat. These studies indicated that oxygen perfused in the gaseous state is utilized by the heart and that cardiac contraction may be maintained for prolonged periods when the heart is perfused with oxygen alone.

In the present studies gaseous oxygen was

perfused in a retrograde direction into the coronary sinus with maintenance of the heartbeat for prolonged periods. The chief difference noted in these studies when contrasted with arterial perfusion was in the strength of cardiac contraction. The beat was observably weaker and extended for a shorter period of time than in the preparations perfused through both coronary arteries.[10] However, the results indicate that gaseous oxygen is utilized when perfused in a retrograde manner through the myocardial vascular bed.

SUMMARY

In an experimental study the isolated heart of the dog has been perfused with gaseous oxygen in a retrograde manner through the coronary sinus. Under these circumstances the heart continued to beat for periods from 2 to 5½ hr. These observations indicate that the heart is able to utilize gaseous oxygen perfused retrograde through the myocardial vascular bed.

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REFERENCES

1. Beck, C. S. Stanton, E., Batiuchok, W., and Leiter, E.: Revascularization of the heart by graft of systemic artery into the coronary sinus. J. A. M. A., *137:* 436, 1948.
2. Blanco, G., Adam, A., and Fernandez, A.: A direct experimental approach to the aortic valve. II. Acute retroperfusion of the coronary sinus. J. Thoracic Surg., *32:* 171, 1956.
3. Bunzl, A., Burgen, A. S. V., Burns, B. D., Pedley, N., and Terroux, K. G.: Methods for studying the reflex activity of the frog's spinal cord. Brit. J. Pharmacol., *9:* 229, 1954.
4. Burns, B. D., Robson, J. G., and Smith, G. K.: The survival of mammalian tissues perfused with intravascular gas mixtures of oxygen and carbon dioxide. Canad. J. Biochem. & Physiol., *36:* 499, 1958.
5. Gott, W. L., Gonzalez, J. L., Zuhdi, M. N., Varco, R. L., and Lillehei, C. W.: Retrograde perfusion of the coronary sinus for direct-vision aortic surgery. Surg. Gynec. & Obst., *104:* 319, 1957.
6. Gregg, D. E., Shipley, R. E., and Bidder, T. G.: The anterior cardiac veins: their functional importance in the venous drainage of the right heart. Am. J. Physiol., *139:* 732, 1943.
7. Magnus, R.: Die Thätigkeit des Überlebeuden Säugethierherzens bei Durchströmung mit Gasen. Arch. Path. Pharmakol., *47:* 200, 1902.
8. Pratt, F. H.: The nutrition of the heart through the vessels of thebesius and the coronary veins. Am. J. Physiol., *1:* 86, 1898.
9. Roberts, J. T., Browne, R. S., and Roberts, G.: Nourishment of the myocardium by way of the coronary veins. Fed. Proc., *2:* 90, 1943.
10. Sabiston, D. C., Jr., Talbert, J. L., Riley, L. H., Jr., and Blalock, A.: Maintenance of the heart beat by perfusion of the coronary circulation with gaseous oxygen. Ann. Surg., *150:* 361, 1959.

HYPERTROPHIC PYLORIC STENOSIS IN ADULTS*

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Pyloric stenosis, occurring in adults, usually is caused by gastric or duodenal ulceration or by carcinoma. In fact, in a recent study,[1] other causes for pyloric stenosis were found in only 3 of 118 adult patients. There are a number of rare conditions which may cause obstruction at the pylorus and one of these, even in adults, appears to be the result of hypertrophy of the pyloric musculature. Although the adult form of this condition was observed and described many years ago by Portal and by Cruveilhier, North and Johnson[3] were able to find only 59 cases in the literature by 1950. To these they added 5 of their own. A more recent report[4] adds 6 additional patients who were thought to have this condition.

As to be expected, the chief symptom of this condition is vomiting. There may also be rather ill defined, ulcerlike symptoms of long duration. Unfortunately, radiologic diagnosis of this condition is not readily made, although delayed emptying of the stomach is observed in some instances. Even at laparotomy, the condition may escape detection or may be thought to be simply a thickened pylorus secondary to chronic ulceration; the true state of affairs is likely to be arrived at only if the pylorus is removed for examination or if, at least, a biopsy of the pylorus taken.

There would appear to be no complete agreement as to the etiology of this condition. The pyloric hypertrophy is not as large proportionately in the adult as is the congenital type of hypertrophy in the infant. In all of the acceptable cases, however, the pyloric muscle is described as being several times larger than normal, and there is usually some comment upon the thinning of the mucosa and the scarring of the submucosa in this area. Peptic ulceration is absent, and evidence of recent gastric or duodenal ulceration in the vicinity of the pylorus is usually not found. The appearance is that of simple hypertrophy and does not suggest neoplasia.

During the past 2 years the author has had occasion to operate upon 3 patients who were found to have pyloric hypertrophy. In all 3 instances the complaint was vomiting of a persistent nature; each of these patients had associated lesions to which the vomiting had been ascribed before surgery. Furthermore, 2 of these patients had had previous operations which failed to relieve the complaint.

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CASE REPORTS

Case 1. T. J. (JHH695711), a Caucasian man, 43 years old and married, was admitted to the Johns Hopkins Hospital June 17, 1957. His general health in the past had been reasonably good. He had had a right inguinal hernia repaired at the age of 26 and had undergone hemorrhoidectomy at the age of 34. Seven years before this admission, he began to have frequent eructation, mild epigastric pain and occasional nausea. He found that the symptons were made worse by lying down and that at night he felt a pressure against his heart. As time went on, he began to have occasional episodes of vomiting which led to a diagnostic study 2 years before the present admission. At that time he was observed to have, on radiologic examination, a small esophageal hiatus hernia; this same examination also disclosed irregularity of the duodenal bulb, but no ulcer crater was noted. After the diagnosis of hiatus hernia, a transthoracic repair was carried out. For about a year the patient was relieved of his symptoms but then began to have recurrent nausea and daily vomiting. The ability to maintain his usual weight was an indication of incomplete obstruction.

Esophagoscopic and roentgenologic examinations did not reveal any recurrence of the hiatus hernia, but the duodenal irregularity was again noted. It was now thought that the patient probably had a duodenal ulcer, which presumably was present at the time of the original operative procedure. For this reason, laparotomy was performed on June 18, 1957, at which time it was apparent that there was no recurrence of the hernia. There was no evidence of either gastric or duodenal ulceration. However, the pylorus was obviously thickened and constricted. A longitudinal incision was made through the full thickness of the stomach, pylorus, and first part of the duodenum. Again, the fact that no peptic ulcera-

tion was present was confirmed. A small portion of the incised stomach and duodenum, including the pylorus, was removed for section, and the opening, which had been made parallel to the long axis of the lumen, was then closed in a trans verse direction, thus accomplishing a Heinecke-Mikulicz type of pyloroplasty. Microscopic examination of the specimen removed revealed marked hypertrophy of the pyloric musculature. The patient left the hospital without further incident on June 27, 1957, and has had no recurrence of his symptoms.

The occurrence of symptoms from an esophageal hiatus hernia in association with a chronic duodenal ulcer is not unusual, and it has been pointed out before now that the repair of the hernia will not regularly relieve such symptoms if the function of the pylorus remains impaired. In fact, Burford[2] believes that a gastric drainage operation in patients having a short esophagus is more helpful than the repair of the hiatus hernia. It is not surprising that there was persistence of symptoms in the case of the patient referred to above, although the cause of the pyloric stenosis was an uncommon one. This experience enabled the author to recognize the lesion in the following patient.

Case 2. S. L. (JHH759702), a Caucasian man, 40 years old and married, was admitted to the Johns Hopkins Hospital on January 24, 1959. He had sustained numerous injuries to his extremities in World War II. At the age of 27 he had undergone appendectomy. His presenting complaint was persistent vomiting of 18 months' duration. The story of the vomiting was somewhat unusual in that the patient stated that it occurred daily and usually in the morning. At first he was able to maintain his weight but in recent weeks he lost 15 pounds. Roentgenographic studies disclosed a small hiatus hernia, one moderate-sized stone in the gall bladder, and what was described by the radiologist as a "spastic duodenal bulb." The patient did not complain of pain but, on questioning, admitted to some discomfort when lying flat after dinner. He said that he would frequently get up at night because of a feeling of fullness or pressure, which was relieved by assuming the upright position.

Operation was undertaken on January 28, 1959, employing an upper midline abdominal incision. The radiologic findings of a small hiatus hernia and a gallstone were confirmed. No ulcer could be demonstrated in the stomach or duodenum, but it was at once observed that the pyloric ring was unusually dense and tight, resembling very much that seen in infantile hypertrophic pyloric stenosis. Cholecystectomy was performed first; then, the esophageal hiatus hernia was repaired. The final part of the procedure was to incise the pylorus longitudinally, removing a small portion of the pyloric musculature for study. The pyloric incision was closed in a transverse direction. The postoperative course was satisfactory, and the patient's symptoms have been completely relieved. Examination under the microscope of the portion of pylorus indicates benign hypertrophy of the pyloric musculature with some scarring of the submucosal layer. The patient was discharged on February 10, 1959.

One is tempted to wonder, in view of the above experiences, whether or not pyloric hypertrophy of this kind may be more than occasionally responsible for a failure to relieve the symptoms of hiatus hernia after an anatomically successful repair. In addition, it certainly seems wise to attempt the repair of a diaphragmatic hernia transabdominally whenever there is any question of pyloric stenosis. It is also perfectly reasonable to entertain some doubt as to the significance of the esophageal hiatus hernia as the cause of symptoms in both of these patients. Furthermore, as will be seen from the case report of the 3rd patient, which follows, the possibility exists that this pyloric lesion may be responsible for symptoms even though some measure of gastric emptying has already been established.

Case 3. A. R. E. (UMH140839-3), a Caucasian woman, 40 years old and married, was admitted to the Union Memorial Hospital on October 19, 1958, because of intractable vomiting. It was of interest that one brother had had gastric surgery, also because of vomiting. The patient's present illness began at the age of 25, over 15 years before the present admission. During this period she always had had poor appetite, nausea and frequent vomiting, usually vomiting large amounts. She underwent exploratory laparotomy at the age of 28; there were no significant findings, and there was no improvement in her symptoms. Seven years before this admission, at the age of 33, the patient was again explored because delay in gastric emptying had been noted on fluoroscopy. Because of this radiologic observation a posterior gastroenterostomy was performed, although the surgeon did not recognize any lesion of the stomach or duodenum at the time of operation. Again, the patient's symptoms were not relieved. Amazingly enough, the patient was always able to maintain her nutrition despite the frequent vomiting.

On the present admission radiologic studies indicated a well visualized gall bladder which emptied normally, the colon as shown by barium enema appeared normal, and studies of the upper gastrointestinal tract indicated that the lower portion of the stomach was either absent or did not fill. The gastroenterostomy appeared to function adequately.

A t operation, on November 25, 1958, thickening of the pyloric musculature with nearly complete stenosis of the canal was observed. The gastroenterostomy was taken down, and the jejunum closed. A resection of the lower half of the stomach was carried out and continuity restored by a Billroth I procedure. Microscopic study of the specimen indicated submucosal scarring with massive hypertrophy of the pyloric muscle. The patient was discharged on December 14, 1958, and has been completely asymptomatic since operation.

In view of the rather uncommon occurrence of pyloric hypertrophy in adults, it is not remarkable that the proper diagnosis was not made in the two laparotomies which preceded the final operation. One must confess to surprise, however, at the failure of the drainage operation to provide relief of symptoms. Vomiting was the principal symptom in all 3 of the patients reported above, as it has been in most of the previously recorded reports. It is possible that both the vomiting and the pyloric hypertrophy are the result of some as yet undisclosed disturbance of normal gastric physiology. Why the symptoms were relieved by resection of the pylorus, or by division of the pylorus, but were unrelieved by posterior gastroenterostomy remains an unanswered question. This experience is not unique, however; of the 5 new cases reported by North and Johnson,[3] the 3 patients who underwent resection had good results.

SUMMARY

It would appear that benign pyloric hypertrophy occurring in adults, of which the most common symptom is persistent vomiting, can be symptomatically relieved by pyloroplasty or by pyloric resection. Case reports of three patients, who are believed to have suffered from this condition, have been presented, two of whom had the additional finding of small esophageal hiatus hernia. It is thought that the diaphragmatic hernia in these two patients, in retrospect, was not the cause of the patients' complaints. The transabdominal approach to the repair of esophageal hiatus hernia is recommended whenever vomiting is a major complaint.

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REFERENCES

1. Balint, J. A., and Spence, M. P.: Pyloric stenosis. Brit. M. J., No. 5126: 890, 1959.
2. Burford, T. H., and Lischer, C. E.: Treatment of short esophageal hernia by Finney pyloroplasty. Ann. Surg., *144:* 647, 1956.
3. North, J. P., and Johnson, J. H., Jr.: Pyloric hypertrophy in the adult. Ann. Surg., *131:* 316, 1950.
4. Skoryna, S. C., Dolan, H. S., and Gley, A.: Development of pyloric hypertrophy in adults in relation to the structure and function of the pyloric canal. Surg. Gynec. & Obst., *108:* 83, 1959.

TWO UNUSUAL URETHROPLASTIES*

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The purpose of this brief report is to present two unusual urethroplasties, each embodying a different principle, with the hope that in the rare instances in which they may be applicable, they will be considered. The author is deeply indebted to Mr. William P. Didusch and Mr. Leon Schlossberg for their superb illustrations.

METHOD 1

The first method is best described as an intubated ureterotomy and anastomosis of an accessory (or duplicated) urethra to the distal portion of a normally situated urethra, part of which was involved in stricture.

This boy was first seen here in September 1949 at the age of 4 months. The mother related that at birth the infant voided through an opening in front of the rectum. Examination of the penis by the obstetrician revealed a dimple present where the urethral meatus is situated normally. However, within a week this dimple opened and urine could be seen coming from it. Since that time the infant had passed varying amounts of urine through both orifices.

Appropriate examinations were conducted and revealed the anatomy shown in figure 1. During micturition all of the urine could be made to come from either the normally situated meatus or the perineal orifice by closing one or the other with a finger. Between voidings the infant was continent, indicating that the external urethral sphincter functioned normally and that the limb of the duplicated urethra which opened in the perineum arose from the normally situated urethra distal to the sphincter.

In December 1949, when the infant was 6 months old, an attempt was made to remedy the difficulty by high closure of the duplicated urethra after dissecting it away from the rectum. Urine was diverted for a time by suprapubic cystostomy. This effort was not successful and within a few weeks the original pattern of voiding varying amounts from each orifice returned. Failure of this procedure indicated a more severe narrowing of the pendulous portion of the normally situated urethra than judged initially. A decision was made to postpone further attempts until the child was older.

He was readmitted here in April 1954 at the age of 5 years. He was again observed to void through the 2 orifices described, but most of the urine came from the perineal opening. The stream from the normally situated meatus was indeed small, reminiscent of the stream from a no. 25 gauge hypodermic needle.

An extensive examination was conducted under anesthesia and revealed the following points of significance. A no. 10 F infant sound could be passed through the first portion of the normally situated urethra, but not beyond (points *A* to *B*, fig. 1). The accessory urethra admitted a no. 10 F sound, and a no. 10 F catheter passed easily into the bladder and obtained clear urine. This urethra paralleled the rectum for a distance of fully 2 cm. (points *F* to *E*, fig. 1), and rectal palpation with a sound in this urethra suggested that no more than a few millimeters of tissue separated the rectum from this urethra. Efforts to visualize a communication between the 2 urethras with an infant panendoscope were unsuccessful, nor could the entire anatomy be demonstrated with opaque media and x-rays.

At operation on April 9, 1954, these findings were confirmed and additional information gained. Again a no. 10 F sound could be passed a distance of 3.5 cm. through the normally situated urethra, but again met an impassable obstruction. A no. 5 F ureteral catheter was then passed through this urethra as far as it would go and indigocarmine injected through it. This dye was immediately seen in the urine obtained by passing a catheter into the bladder through the perineal urethra. The normally situated pendulous urethra was then explored through a midline ventral incision beginning at the point of obstruction to the sound and carried back to the perineal meatus. The strictured portion of the urethra was identified as a thin-walled tube less than 2 mm. in diameter. The corpus spongiosum was poorly developed, permitting one to see the

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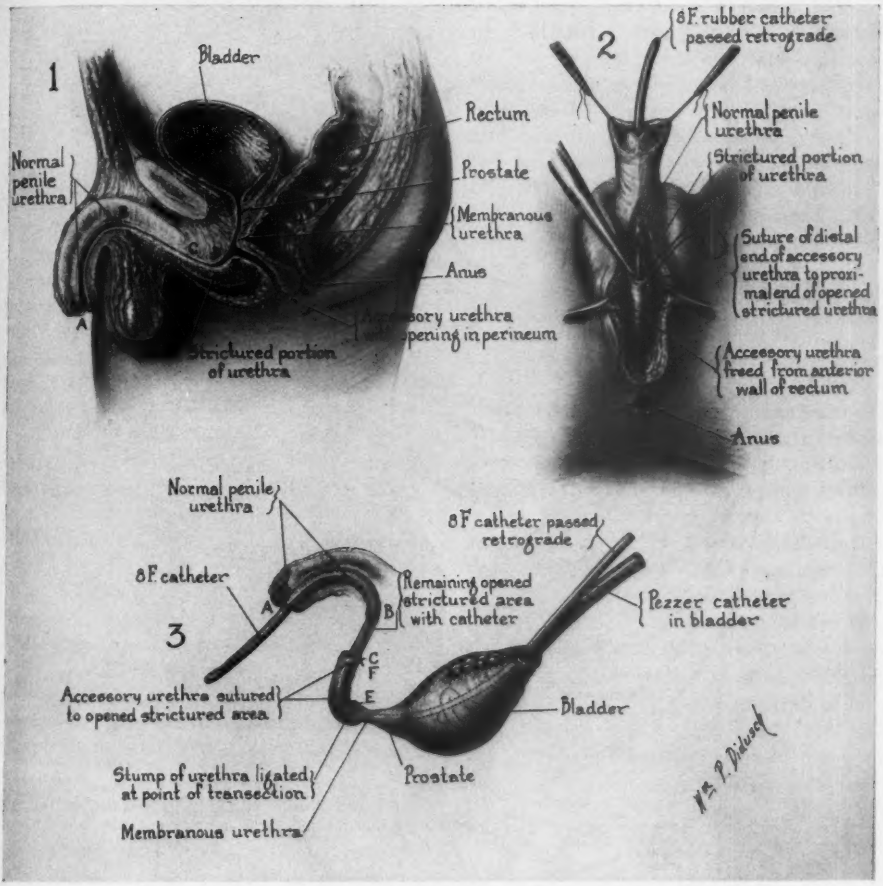


FIGS. 1, 2 AND 3. Method one. Intubated ureterotomy and anastomosis of an accessory urethra to the distal portion of a normally situated urethra.

indigocarmine through the epithelium of the urethra. It was estimated that the atretic portion of this urethra measured 5 cm. in length (points *B* to *C*, fig. 1). The perineal urethra was then mobilized for a distance of 3 to 4 cm. by carefully dissecting it free from the rectum. It was then swung upward in an effort to see whether it would reach to point *B*, figure 1, the most distal point of narrowing of the normally situated urethra. Its length would not permit this, so a decision was made to use all of this accessory urethra, join it to the atretic urethra at a convenient point without tension (points *F* to *C*, figs. 1 and 3), incise the strictured portion longitudinally and intubate it. A suprapubic cystotomy was performed which revealed a normal trigone and a single internal vesical orifice. A no. 8 F red rubber catheter was passed as a splint, placed as shown, and the bladder drained. The proximal portion of the strictured urethra was tied and cut off at the point of junction with the accessory urethra (point *E*, figs. 1 and 3). The wound was closed in layers.

The child's postoperative course was complicated by slight separation of the superficial portion of the perineal wound. On the 21st postoperative day, the suprapubic tube was removed under anesthesia and the urethral splint replaced with a no. 10 F red rubber catheter acting as a drain for urine. Four days later this

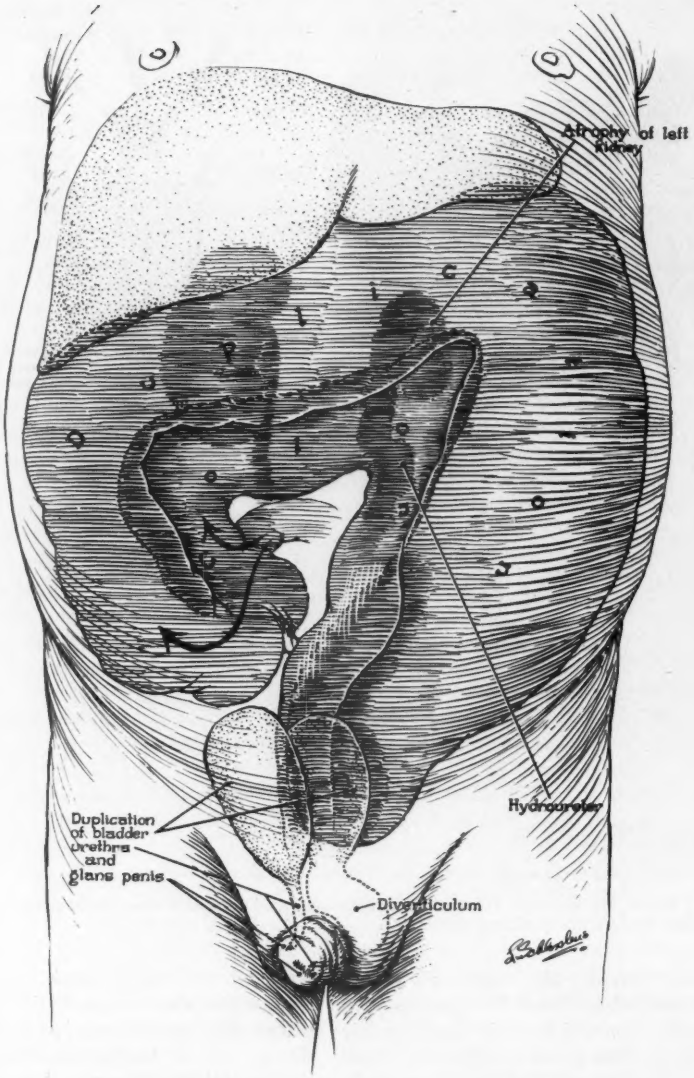


FIG. 4. Schematic drawing to illustrate the condition found in the second child at 4½ years. There is one terminal ileum and one appendix, but the normal colon at the cecum is continuous with an enormously dilated and hypertrophied duplication which parallels the colon and is densely adherent to it as far as the very depth of the pelvis where it ends blindly. The right kidney and ureter are normal. The left kidney is atrophic and its ureter markedly dilated. A septum divides the bladder in two. The right bladder empties by its own urethra through a hypospadiac meatus. The left urethra is involved in a large diverticulum, and its meatus is situated at the tip of a partially duplicated glans. (Reproduced from an article by M. M. Ravitch and W. W. Scott.[1])

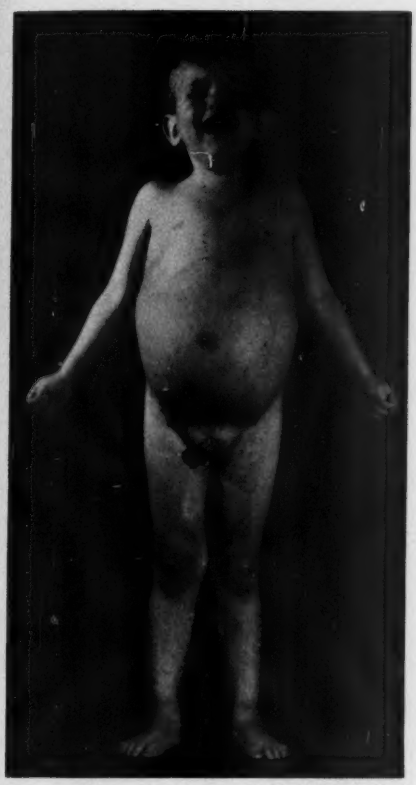


FIG. 5. Illustrating the marked abdominal distention before resection of the reduplicated colon at age 4½ years. (Reproduced from an article by M. M. Ravitch and W. W. Scott.[1])

was replaced with a no. 12 F catheter, which was removed after 6 days. The child, discharged on the 32nd postoperative day, was voiding well through the normally situated meatus. He has subsequently been seen at regular intervals by another urologist and has done exceedingly well. The last note we have received is dated June 17, 1957, and reads, "P. A. R. was in today. The stream size on voiding is excellent and the urine is entirely clear." To date, urethral dilations have never been necessary.

METHOD 2

Method 2 may be summarized as a construction of a single urethra with a normally situated meatus by forming a distal urethra from a duplicated urethra involved in a diverticulum and end-to-end anastomosis of this urethra to a second urethra involved in penile hypospadias.

This patient was the subject of an earlier communication by Dr. Mark M. Ravitch and this author in 1953.[1] A brief summary of his previous admissions follows. He was first seen in this hospital in November 1948 at the age of 4½ years because of a deformity of the penis and severe abdominal distention since birth. Extensive studies revealed duplication of the large bowel, a normal right kidney and ureter, left hydroureteronephrosis, a bladder divided in two by a complete midline septum, 2 internal vesical orifices and 2 urethras (fig. 4). The right urethral meatus was hypospadiac, and the left

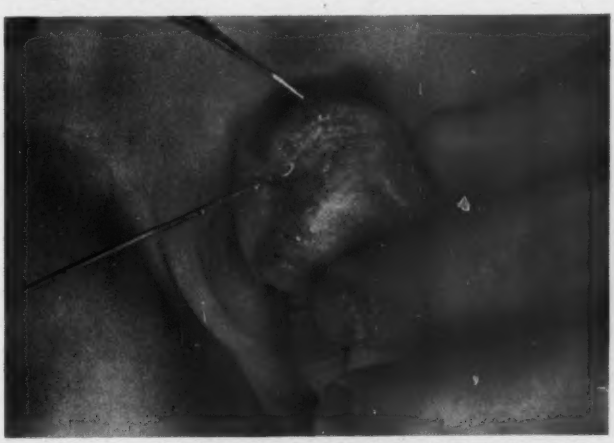


FIG. 6. Close-up of penis at age 4½ years. The upper pointer indicates the orifice of the left urethra which was involved in a diverticulum. The diverticulum itself was filled when this picture was made and can be seen as a bulge between the pointer and the thumb and index fingers of the examiner. The lower pointer indicates the hypospadiac orifice of the right urethra. (Reproduced from an article by M. M. Ravitch and W. W. Scott.[1])

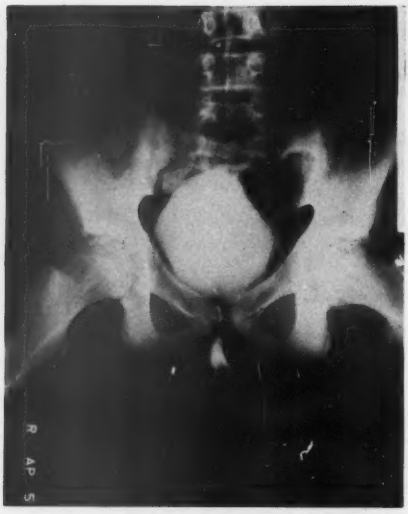


FIG. 7. A contrast cystogram made following left nephroureteroectomy, excision of the bladder septum and closure of the left internal vesical orifice. This film was made following injection of the right urethra and shows a capacious, symmetrical bladder and a meatus of normal caliber. The veru montanum is clearly visible.

opened slightly to the left of the midline at the tip of a glans which was partly duplicated and contained a dimple at the site where the right urethra should have opened. The left urethra in its penile portion was involved in a lemon-sized fusiform diverticulum. Apparently the function of the left kidney was extremely poor but sufficient to fill this urethral diverticulum which emptied at intervals without control. Otherwise he had no urinary complaints.

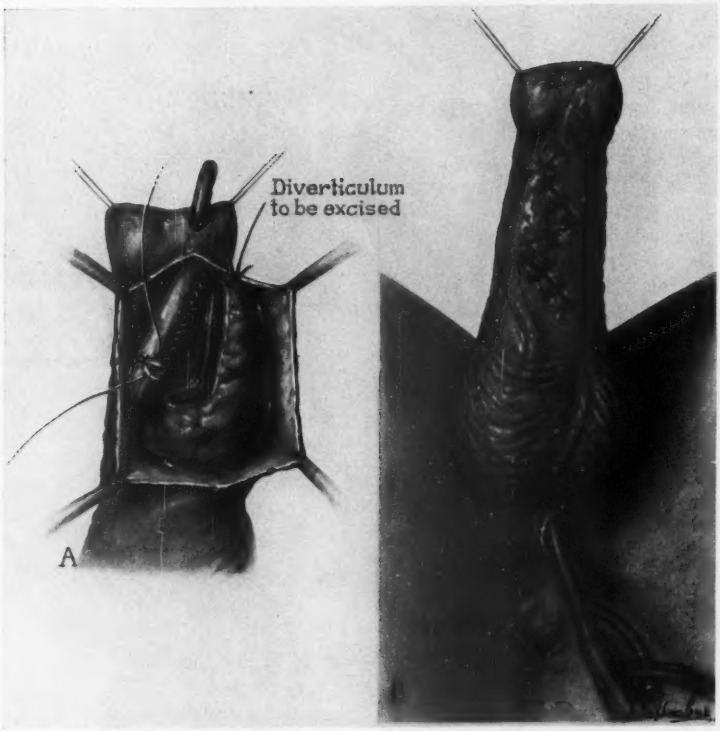
During 2 admissions involving 4 operations, the duplicated colon was resected, the left kidney and ureter were removed, the septum dividing the bladder in two was excised, and the left internal vesical orifice was closed. When discharged from the hospital, he had essentially normal bowel habits and voided all urine from the right hypospadiac urethra with good control and with normal frequency. A decision was reached to postpone plastic reconstruction of the penis and the urethra until the child was older.

The boy was readmitted to this hospital in September 1958. In the interval he had developed into a strong, big boy. He had no complaints except for the appearance of his penis and the fact that the urethra through which he voided all urine was hypospadiac. The diverticulum of the left urethra no longer filled with urine nor secretions. Genital development except for the penis was normal and "nocturnal emissions" were reported to have occurred. Unfortunately, no photographs of the penis were made immediately before reconstructive surgery; however, two were made when the child was first seen at the age of 4½ years (figs. 5 and 6). These help to show the situation, and Mr. Schlossberg's drawings clearly illustrate the anatomy. A contrast cystourethrogram made after injection of the right urethra shows a capacious, symmetric bladder and a urethra of normal caliber (fig. 7). The veru montanum is clearly visible. Injection of the left urethra resulted in an x-ray showing filling of the urethral diverticulum with no communication with the bladder.

At operation, a no. 18 F red rubber catheter was passed easily through the right hypospadiac urethra into the bladder without meeting any obstruction and obtained clear urine. This urethra was opened in its perineal portion and perineal urethrostomy drainage established. The distal end of this urethra was then dissected free for a distance of 2 cm. (fig. 8*A*). Attention was then focused on the left urethra whose meatus opened on the glans. This urethra and its fusiform diverticulum were opened through a ventral incision beginning just proximal to the coronal sulcus, and a tube 4 cm. long and at least 16 mm. in circumference was fashioned from the distal portion as shown in figure 8*B*. The proximal end of this tube was then anastomosed end-to-end with the distal end of the right urethra (fig. 9*A*). The remainder of the diverticulum and proximal left urethra were then excised, together with redundant skin, and Z-closure of the skin of the ventrum of the shaft accomplished (fig. 9*B*). A small inverted V-shaped wedge of tissue was removed from the ventrum of the glans in order to make the glans appear more like a single than a double one and in order to bring the urethral meatus closer to the midline. The anastomosis was not splinted, the only drain being a Foley catheter placed through the perineal urethrotomy.

Healing occurred by first intention. Sutures and catheter were removed on the 9th post-

FIGS. 8*A* and *B*. Method two. (See text for explanation.)



FIGS. 9*A* and *B*. Method two. (See text for explanation.)

FIG. 10. Appearance of the penis on the 12th postoperative day.

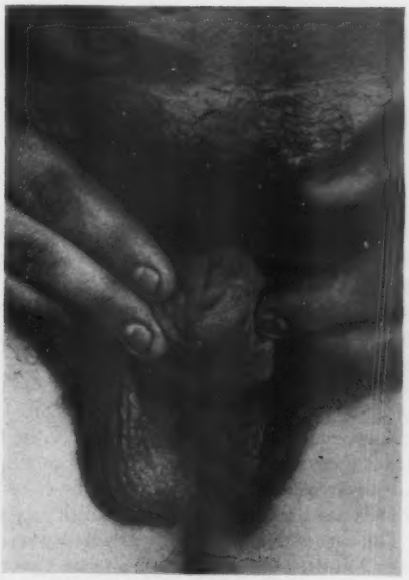


FIG. 12. Appearance of the penis 15 months after operation.

FIG. 11. Illustrating the caliber of the urinary stream on the 12th postoperative day.

operative day, and the boy voided with a full stream thereafter. Figure 10 shows the appearance of the penis on the 12th postoperative day, the day of discharge from the hospital, and figure 11 shows the caliber of the urinary stream.

It is now 15 months since this operation, and the boy continues to void with a good stream, without spraying and with no undue frequency. The urine is normal. Figure 12 shows the appearance of the penis 15 months postoperative.

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REFERENCE

1. RAVITCH, M. M., AND SCOTT, W. W.: Duplication of the entire colon, bladder, and urethra. Surgery, *34*: 843, 1953.

ANATOMICAL VARIATIONS IN 46 PATIENTS WITH CONGENITAL AORTIC STENOSIS*

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This report describes the anatomical variations seen in 46 patients with congenital aortic stenosis and discusses their clinical and surgical significance. The stenosis was supravalvular in one patient, valvular in 24, subvalvular in 13, and combined valvular and subvalvular in 3 (table 1). In 2 patients the stenosis was present in both right and left ventricular outflow tracts, and in 3 patients there was underdevelopment of the left side of the heart. The aortic valve and ventricular outflow tract were examined under direct vision at open heart surgery or at autopsy in all patients.

The ages at time of surgery or autopsy ranged from 2 months to 24 years with a mean age of 10 years (table 1). The sex incidence is interesting in that among the 31 male patients there were only 4 atypical cases, whereas almost 50 per cent of the 15 female patients had associated defects. There was only one Negro in the series.

The clinical picture in the cases operated upon was that of severe aortic stenosis, with symptoms of mild to moderate dyspnea and fatigue in all and angina or syncope in about one-third. In most patients the heart was only slightly enlarged and the physical signs were typical of aortic stenosis; absence of the usual harsh stenotic murmur and thrill in the aortic area was usually associated with a complicated malformation or with the "muscular" type of subvalvular obstruction. The pulse pressure was narrow in the majority of the patients.

Surgical indications were symptoms of dyspnea, angina, or chest pain, and a left ventricular "strain" pattern on the electrocardiogram with ST depression and T-wave inversion. Left heart catheterization was performed in about one-half of the patients, and all had a left ventricular-aortic pressure gradient above 50 to 60 mm. Hg. All except the earliest operations were done with cardiopulmonary bypass with a screen oxygenator.[16] Aspiration of the left atrium through a catheter inserted through the left atrial appendage greatly helped the operative procedure by providing a dry field and by preventing overdistension of the left side of the heart. Potassium induced asystole has been replaced in recent months by intermittent coronary perfusion during the time the aorta is open.

SUPRAVALVULAR AORTIC STENOSIS

Pathologic Anatomy

This is probably the rarest type of aortic stenosis. The obstruction is caused by a fibrous ledge 1 to 2 cm. above the valve. This ledge, which is a projection of fibrous tissue and elastic fibers extending from the media, may completely encircle the aorta to form an annular ring (fig. 1). The valve below may be normal or show only slight thickening of the cusps. In case 1, however, and in 5 of the cases reviewed by Denie and Verheught there was definite thickening of the valve leaflets, producing a mild degree of valvular stenosis in addition to the supravalvular lesion. In case 1 (previously reported by Sissman and associates[14]) the aorta was 4 cm. in circumference at the aortic valve ring but was narrowed to 3 cm. at the site of the supravalvular stenosis; the area of constriction extended over a distance of 2 cm., probably due to fibrosis after a previous attack of subacute bacterial endocarditis. In some of the reported cases the site of stenosis has been visible on the external surface of the aorta as a localized circular narrowing whereas in others the external surface of the aorta has appeared normal.

In some of the cases reviewed by Denie and Verheught[6] one of the coronary cusps has been adherent to the area of supravalvular stenosis with resulting partial obstruction of the orifice of the corresponding coronary artery.

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† John and Mary R. Markle Scholar in Medical Science.

TABLE 1

*46 proved cases of congenital aortic stenosis**

Case No. and Stenosis	Name	Age	Sex	Associated Defects	Operation	Deaths
		yr.				
Supravalvular						
1	P. W.	13	M	Vegetations from bacterial endocarditis	Transventricular	D
Valvular						
2	J. McG.	7	M		Hypothermia	
3	D. P.	13	M		Bypass	
4	R. T.	18	M		Bypass	
5	K. S.	10	F		Bypass	
6	T. D.	3	M	Incomplete right bundle branch block	Bypass	
7	E. H.	10	M		Bypass	
8	A. F.	14	M		Bypass	
9	R. G.	17	M		Bypass	
10	R. M.	19	M	Early calcification	Bypass	
11	J. D.	14	M	History of rheumatic fever; aortic insufficiency (mild)	Bypass	
12	C. W.	10	F		Bypass	
13	R. L.	16	M		Bypass	
14	R. C.	10 mo.	M		Bypass	
15	J. W.	9	M		Bypass	
16	S. A.	5 mo.	F	Coarctation; patent ductus; gonadal dysgenesis	Bypass	D
17	M. R.	11	M		Bypass	
18	W. W.	6	M		Bypass	
19	S. S.	8	F		Bypass	
20	J. R.	8	M		Bypass	
21	F. K.	12	F		Bypass	
22	R. McC.	14	M		Bypass	
23	G. M.	14	M	Dilatation ascending aorta	Bypass	
24	L. H.	3 mo.	F	Coarctation	None	D
25	N. P.	2 mo.	F	Small valve ring; fibroelastosis	None	D
Valvular + subvalvular						
26	R. B.	9	M		Bypass	
27	B. A.	12	F	Coarctation	Bypass	
28	M. McN.	13	F	History of rheumatic fever; mitral insufficiency	None	D
Subvalvular:						
(*a*) *fibrous ring*						
29	P. Q.	8	M		Bypass	
30	W. P.	18	M		Bypass	
31	M. G.	14	M	Aortic insufficiency (mild)	Bypass	
32	G. B.	13	M		Bypass	
33	C. J.	8	F		Bypass	
34	D. vK.	9	F		Bypass	D
35	J. K.	13	M		Bypass	
36	S. L.	17	M		Bypass	D
37	C. F.	14	M	2 small right coronary ostia; left normal	Bypass	
38	J. C.	7	M	Patent ductus	None	D
(*b*) *muscular hypertrophy*						
39	B. W.	15	F	History of bacterial endocarditis	Bypass	
40	W. K.	14	M		Bypass	
41	G. W.	24	M	Aortic insufficiency; "pouch" on mitral valve	Bypass	

TABLE 1—*Continued*

Case No. and Stenosis	Name	Age	Sex	Associated Defects	Operation	Deaths
		yr.				
Combined aortic and pulmonic						
42	J. S.	6	F		Hypothermia	D
43	M. M.	6	M	Ventricular septal defect	Bypass	D
Underdeveloped left ventricle						
44	M. T.	2	F	Left ventricular-right atrial defect; mitral insufficiency	Transventricular	D
45	M. C.	4	M	Mitral valve deformed; fibroelastosis	Bypass	D
46	S. McD.	1 mo.	F	Ventricular septal defect; patent ductus; hypoplastic aorta	None	D

* Cases 1 and 42 reported by Sissman and co-workers,[14] case 44 by Ferencz[8] and cases 3 to 10 and 29 to 32 by Spencer and associates.[16]

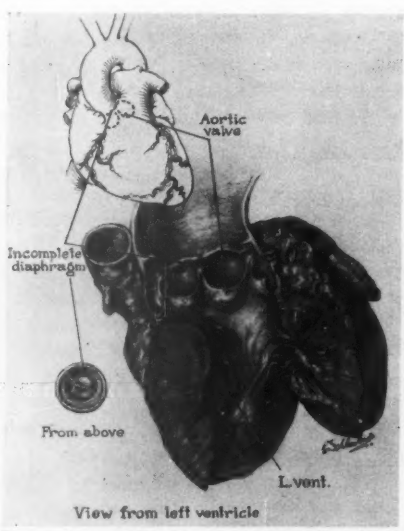

FIG. 1. Supravalvular aortic stenosis, autopsy specimen of 70-year-old patient, who was grandmother of case 1, table 1. Stenosis was not significant in this patient.

Other anatomical variations have included an associated Marfan's syndrome or rheumatic or bacterial endocarditis superimposed on the congenital malformation.

Clinical Considerations

The one patient seen with supravalvular stenosis (case 1, table 1) developed intractable cardiac failure after bacterial endocarditis and died during an attempted transventricular valvulotomy. Fibrosis from endocarditis may have made the degree of stenosis more severe. A much more benign course with a similar type of stenosis in the grandmother of this patient has been previously reported.[14]

The thrill and murmur in the aortic area may be unusually superficial and well transmitted to the cervical vessels. The aortic second sound is normal or slightly diminished. Retrograde left heart catheterization or left-sided angiocardiography offer the only certain means of differentiation from valvular stenosis.

Surgical Considerations

A successful operation for supravalvular stenosis has not been reported. The location of the stenosis, however, as shown in figure 1, is a favorable one for treatment by excision or by widening of the stenotic area by inserting a large patch of prosthetic material.

VALVULAR STENOSIS

Pathologic Anatomy

The stenotic valves were strikingly similar in the majority of patients. Fused valve commissures could be readily identified, but the commissure between the two coronary cusps was often incompletely formed; so the valve was functionally a bicuspid one. The differences from a true

bicuspid valve have been analyzed by Abbott.[1] There was usually complete fusion of the coronary commissure, partial fusion of the commissure between the right coronary cusp and the noncoronary cusp, and slight fusion of the commissure between the left coronary and the noncoronary cusps (fig. 2). In all of the stenotic valves the appearance of the fused commissures was that of an incomplete separation of the cusps; none of the valves appeared to have well developed commissures that had "fused" as a result of an inflammatory process. The diameter of the stenotic valve orifice in the cases operated upon ranged from 3 to 6 mm. (table 3) in most patients.

About 30 per cent of the patients had significant variations from the typical pattern described above; these included thickening of the valve cusps, hypoplastic valve ring, subvalvular stenosis, and coarctation of the aorta (table 2). *Thickening of the valve cusps* from the usual 1 mm. or less to 2 mm. or more was present in 6 patients. *Calcification* of the cusps was found only in one 19-year-old boy, one of the oldest patients in the series. Two patients had a *hypoplastic valve ring* that significantly obstructed the outflow tract. The most severe hypoplasia in these 2 patients was seen in a 2-month-old infant (case 25, table 1) whose valve circumference was less than 14 mm.; the stenotic valve orifice was 2 mm. in diameter. Three patients had *subvalvular stenosis* in addition to valvular stenosis, and three had *coarctation* of the aorta.[15] Two of the three patients with coarctation died in infancy.

As is indicated in table 2, multiple abnormalities were often found in the same patient. The four infants in the series had the highest incidence of multiple abnormalities (case 14, 16, 24 and 25, table 1). Only 1 patient, case 14, had a typical valvular stenosis and was successfully operated upon at 10 months of age. Of the 2 patients who died before operation could be attempted (cases 24, 25), one had a hypoplastic ring, and the other nodular thickened valve cusps and a coarctation. Case 16 with a *grossly malformed valve* died at operation; she also had gonadal dysgenesis, a hypoplastic outflow tract, a coarctation of the aorta, and a patent ductus arteriosus.

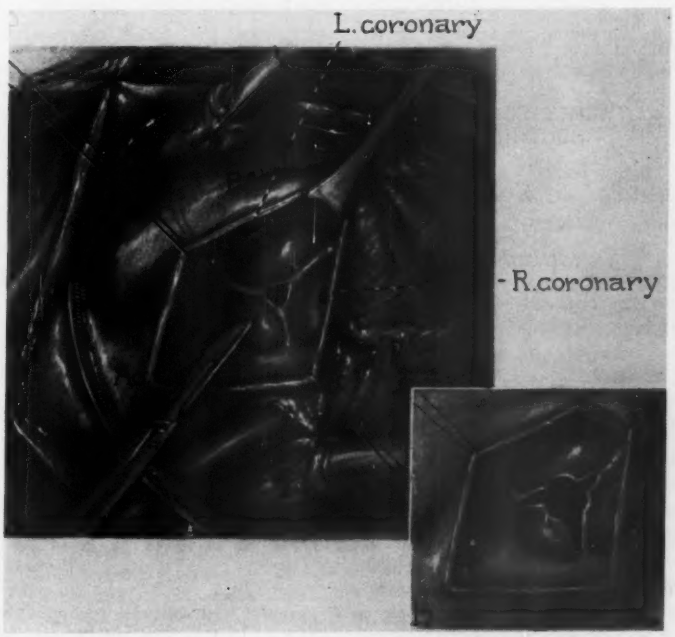

FIG. 2.*A*. Valvular aortic stenosis exposed with incision in ascending aorta. The aorta is occluded distally; cannulae are in the right and left atria. (*B*). Aortic valve after incision of commissures. The coronary commissure is not opened completely if it is not well formed.

TABLE 2

Variations and additional malformations present in 27 patients with valvular aortic stenosis

Malformation	No. of Patients	Case No.
Thickened aortic valve cusps	2	7, 23
Thickened cusps; hypoplastic aortic valve ring	1	15
Thickened cusps; subvalvular stenosis	1	26
Thickened cusps; atrophic cusps; subvalvular stenosis; coarctation	1	27
Thickened cusps; coarctation	1	24
Subvalvular stenosis	1	28
Hypoplastic aortic valve ring	1	25
Grossly deformed valve; coarctation	1	16
Calcification of valve cusps	1	10

Clinical Considerations

The clinical syndrome has been frequently reviewed.[4, 5, 10, 12, 17] Only a few points of surgical interest will be mentioned here. The age incidence of cases requiring operation varied from a few months to 19 years, a range considerably wider than that seen in the subvalvular group (fig. 3). An infant or young child with heart failure or angina from aortic stenosis was much more likely to have the valvular than the subvalvular type. The sex incidence was predominantly male with 17 males and 7 females; if the uncomplicated cases only are included, the male-female ratio is 17 to 4. Poststenotic dilation of the aorta was seen more commonly in this group than in any other and was best diagnosed by fluoroscopy in the left anterior oblique position; gross dilation involving the whole ascending aorta was seen in only 1 case and may have been due to an associated medial necrosis.[9] Aortic insufficiency was seen before operation in only 1 patient (case 11, table 1) with valvular stenosis and was unchanged after operation.

Surgical Considerations

The stenotic valve was exposed with an incision in the ascending aorta and the fused commissures incised with a knife. The method of incision of the commissures is shown in figure 2. It was felt important to incise carefully along the center of the commissural ridge so that each cusp would have a thickened edge that would provide a broad area for coapting and thus lessen the hazard of aortic insufficiency. In 15 of 23 operations the fused commissures were not

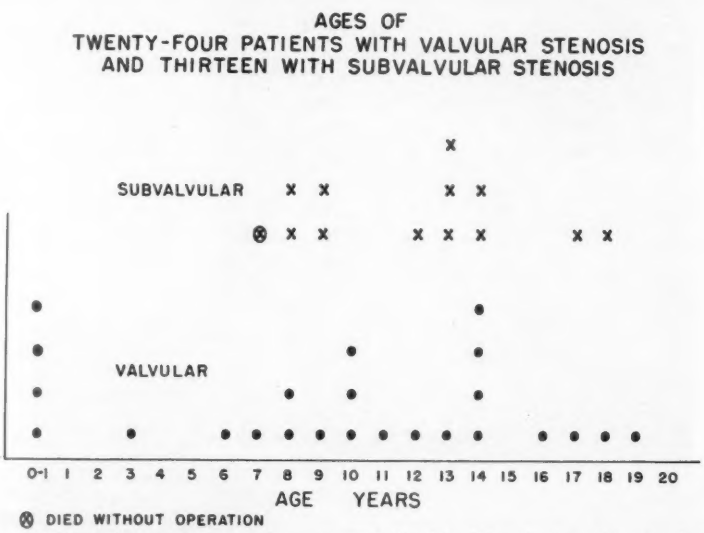

FIG. 3. Ages at time of operation or autopsy in 37 patients with valvular and subvalvular stenosis. Each ● represents 1 patient with valvular stenosis; each x 1 patient with subvalvular stenosis. The 7-year-old patient with subvalvular stenosis, the youngest in the series, was the only one with subvalvular stenosis who died without operation.

opened completely because incision in a poorly developed commissure was thought to carry too great a risk of aortic insufficiency. The commissure that was not opened completely was almost always the one between the two coronary cusps; thus the valve after valvulotomy was essentially a bicuspid one. A limited valvulotomy adequately relieved the obstruction in almost all patients. The diameter of the stenotic valve orifice with the resulting pressure gradient both before and after valvulotomy is shown in table 3. It should be emphasized that the diameters are only approximations as they were estimated and not measured, but the range of values indicates that the usual orifice is between 3 and 6 mm. with a pressure gradient of 60 to 120 mm. Hg. The opening after valvulotomy was usually large enough to admit easily the index finger of the surgeon, which corresponded to a diameter of about 20 mm. An interesting lack of correlation between the size of the stenotic orifice and the severity of symptoms was particularly striking in case 22, a 14-year-old boy with an 8-mm. orifice and a 100-mm. gradient. He had a severe degree of cardiac enlargement with a cardiothoracic ratio of 66 per cent, and symptoms of congestive failure.

TABLE 3

Aortic valve orifice diameter and pressure gradient before and after valvulotomy*

Case No.†	Before Valvulotomy		After Valvulotomy	
	Diameter of opening	Left ventricular-aortic pressure gradient	Diameter of opening	Left ventricular-aortic pressure gradient
	mm.	*mm. Hg*	*mm.*	*mm. Hg*
16	2	80	10	—
3	3	70	20	—
6	3	60	16	0
5	3	66	20	11
7	3	122	16	28
4	4	115	20	46
14	4	70	12	80
15	4	80	12	50
19	4	70	12	0
20	5	125	15	0
8	5	42	16	
11	5	60	20	0
18	5	100		0
9	6	52	20	18
12	6	80	17	0
13	6	40	20	0
17	6	60	13	0
22	8	100	20	25
21	9	100	16	0

* Diameter was estimated visually and by insertion of finger.

† Table 1.

Aortic insufficiency followed valvulotomy in only 5 of 23 operations. One of these 5, an infant, had a grossly deformed valve, one had all of the commissures completely incised, and another had thickened deformed cusps that may have contributed to the insufficiency. There were no deaths after valvulotomy in 22 patients with an uncomplicated valvular stenosis.

Three patients had *combined valvular* and *subvalvular stenosis* (cases 26, 27 and 28, table 1). Two of the three patients had thickened valve cusps in addition to subvalvular stenosis. Both patients operated upon did well.

SUBVALVULAR STENOSIS

Pathologic Anatomy

Subvalvular stenosis was seen as an isolated lesion in 10 patients and in combination with valvular stenosis in 3 patients (table 1). A narrow ring of fibrous tissue was uniformly found at the stenotic area without evidence of stenosis proximal or distal to it (fig. 4). A long stenotic area was seen only in 2 patients with associated pulmonary stenosis and is discussed in that section.

The stenotic orifice was usually 4 to 8 mm. in diameter with a pressure gradient of 70 to 120 mm. Hg (table 4). The distance of the stenotic ring from the aortic valve varied from less than 1 cm. to 3 cm. (table 5). In 1 patient the base of the noncoronary cusp was adherent to the stenotic ring and may have caused the mild aortic insufficiency that was present.

Three patients (cases 39, 40 and 41, table 1) were thought to have stenosis due to "muscular hypertrophy" of the left ventricle. Two of these, cases 39 and 40, were explored during potassium asystole without finding any obstructing lesion. Patient 41 was explored with coronary perfusion and an actively contracting heart but still without the detection of any definite obstruction although a 60 mm. Hg gradient had been present before operation. A pouchlike diverticulum on the aortic leaflet of the mitral valve was present but was so mobile it was thought to be displaced

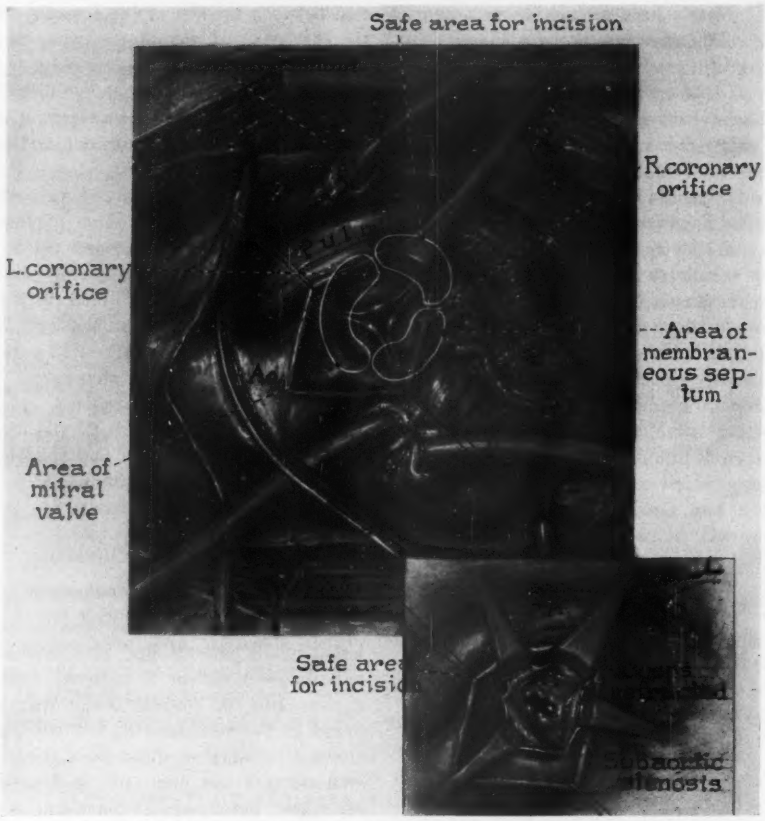

FIG. 4. A normal aortic valve exposed with an incision in the ascending aorta. The areas of the subjacent aortic leaflet of the mitral valve, the membranous ventricular septum, and the left ventricular outflow tract are shown diagrammatically in relation to the aortic valve. The aorta is occluded distally; cannulae are in the right and left atria. The insert shows a subvalvular stenosis exposed by retracting the aortic cusps and indicates the area where the mitral valve or the ventricular septum will not be injured during excision of the stenotic area and adjacent hypertrophied muscle.

toward the left atrium during systole. Moderate aortic insufficiency present before operation in this patient was thought to be caused by downward displacement of the noncoronary cusp by fibrous tissue.

Clinical Considerations

The 10 patients with subvalvular stenosis due to a fibrous ring ranged in age from 7 to 18 years (fig. 3). The age distribution indicates that subvalvular stenosis rarely causes serious difficulty in infancy, but does so between 5 and 20 years of age. The development of serious difficulty may result from progressive muscular hypertrophy and "strain" on the left ventricle. We have not yet seen a patient older than 18 years with subvalvular stenosis.

The accurate clinical differentiation of valvular stenosis from subvalvular was difficult. If a good aortic second sound was present, subvalvular stenosis could be diagnosed with fair confidence; but if it were absent, the diagnosis rested on the comparative rarity of poststenotic dilation or on the shifting character of the murmur, which may be heard down the left sternal border in early childhood rather than in the aortic area. Case 38 had been followed elsewhere without the correct diagnosis being considered because of the atypical position of the murmur and the presence of right axis deviation; the latter is not excessively

TABLE 4

Diameter of subvalvular stenosis and pressure gradient before and after excision*

Case No.†	Before Excision		After Excision	
	Diameter	Left ventricular-aortic pressure gradient	Diameter	Left ventricular-aortic pressure gradient
	mm.	*mm. Hg*	*mm.*	*mm. Hg*
29	4	210	17	146
30	4	34	20	61
31	5	116	20	52
32	5	63	20	0
34	6	120	20	—
35	7	70	20	20
36	7	—	20	10
26	8	75	—	0
27	12	100	15	50
33	15	70	20	7
37	—	50	20	0

* Diameter was estimated visually and by insertion of finger.

† Table 1.

TABLE 5

Distance of subvalvular stenosis from aortic valve in 12 patients

Distance	No. of Patients	Case No.*
cm.		
Adjacent; cusp attached to stenosis	1	36
Adjacent	2	31, 38
1	4	29, 33, 34, 35
1–2	2	26, 27
2	1	32
3	2	30, 37

* Table 1.

rare and does not exclude aortic stenosis provided left ventricular hypertrophy is present. This child was admitted to the Harriet Lane Home in his first and fatal attack of pulmonary edema and died before any studies could be undertaken.

Aortic insufficiency of mild degree was present in 4 of the 10 patients (cases 30, 31, 36 and 37, table 1). In case 36 the noncoronary cusp was adherent to the stenotic ring; in case 37 there was a fibrous band between the stenotic ring and the valve. In the other 2 no cause for the insufficiency could be found, but the signs of aortic insufficiency have regressed since operation.

Subvalvular stenosis due to "muscular hypertrophy" or "pseudo-aortic stenosis" has only recently been recognized.[3] A familial incidence has been emphasized by Bercu and associates[2] and by Morrow and Braunwald.[11] In only 1 of the 3 cases here presented (case 41) was the murmur "typical" of aortic stenosis; in both the others the murmur, although stenotic in type, was less harsh and more diffuse than usual. The aortic second sound was present in all, and the pulse pressure was not unusually narrow. Severe progressive left ventricular hypertrophy in the electrocardiogram occurred in all 3; in 2, left heart catheterization showed a pressure gradient of about 50 mm. Hg between the left ventricle and femoral artery. Left heart catheterization with localization of the stenosis 4 cm. or more below the valve may suggest the diagnosis. The pressure tracing in such a patient is shown in figure 5; this patient is not included in table 1 because the diagnosis has not been proved by surgical exploration of the left ventricle. Cineangiocardiography may prove to be the best diagnostic method.

Surgical Considerations

A subvalvular stenosis was readily exposed through an incision in the aorta by retracting the aortic valve cusps. Aspiration of the left atrium through a catheter previously inserted through the left atrial appendage was of great benefit in obtaining a dry field and thus avoiding injury to adjacent structures during excision of the subaortic stenosis. The location of these vital structures adjacent to a subaortic stenosis is shown in figure 4. A small amount of hypertrophied muscle was excised in some patients after the fibrous ring had been removed; the safe area for excision of muscle in the left ventricular outflow tract is in a limited segment of the periphery of the subaortic ring (fig. 4). Landmarks identifying the location of this area are the commissure between the two coronary cusps and the pulmonary artery just distal to the pulmonary valve.

The stenotic area was excised with a knife, scissors or rongeurs to a diameter of 2 cm. or more. The obstruction as measured by the pressure gradient (table 4) was satisfactorily relieved in all but one patient (case 29, table 1). This patient

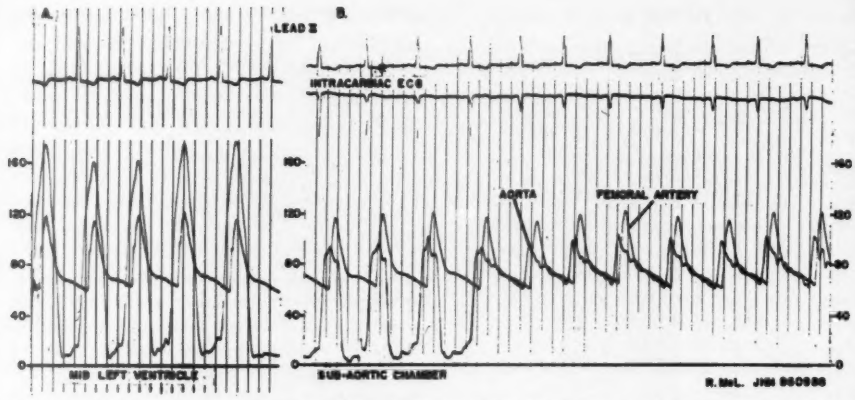

FIG. 5. Simultaneous pressure tracings from femoral artery and from a catheter withdrawn from the ventricle into the aorta in a patient thought to have "muscular obstruction" of the left ventricular outflow tract. On fluoroscopy the area of obstruction was farther down in the ventricle than is usually seen in subvalvular stenosis from a fibrous ring.

has had progressive clinical improvement in the 2 years after operation which may indicate progressive reduction of the residual left ventricular obstruction from a regression of muscular hypertrophy.

There were 2 deaths following 9 operations for subvalvular stenosis. One patient died at operation from injury to the ventricular septum, and one died from left ventricular failure with pulmonary edema 3 days after operation; a severe degree of replacement of the left ventricular muscle by fibrous tissue was found in this patient. There were no injuries to the mitral valve.

There were no deaths in the 3 patients with presumed "muscular" obstruction of the outflow tract. In one the electrocardiogram regressed toward normal in the ensuing year; in the other two the findings are unchanged.

COMBINED AORTIC AND PULMONIC STENOSIS

Clinical Considerations

The unusual combination of stenotic lesions in both ventricles was present in 2 patients (cases 42, 43, table 1). Case 42 has been previously described in detail;[14] the correct diagnosis was not made in life although in retrospect it clearly should have been. The condition should be suspected in any patient with good signs of pulmonary stenosis who has no evidence of a left to right shunt but nevertheless shows left ventricular hypertrophy; or conversely, in any patient with signs of aortic stenosis in whom the pulmonary second sound is diminished and there is right ventricular hypertrophy. The following brief report of case 43 illustrates some of the diagnostic points.

Case 43. M. M. (HLHB-40546), a 6-year-old Caucasian boy, had been treated for congestive failure at 23 months of age but subsequently had only slight dyspnea on exertion. He had small pulses in all extremities with a blood pressure of 90/70 mm. Hg. A harsh grade IV systolic murmur was heard at the base of the heart on both sides of the sternum and was slightly louder on the left; it was well transmitted to the neck and back. The second sound in both pulmonic and aortic areas was almost inaudible. Fluoroscopy showed moderate enlargement of both right and left ventricles. The electrocardiogram showed right axis deviation, incomplete right bundle branch block and right ventricular hypertrophy with some left ventricular hypertrophy. The R in VI measured 4 mm.; the R′, 20 mm.; the S in VI, 9 mm.; the R in V6, 18 mm.; and S, 11 mm. Combined pulmonic and aortic stenosis was diagnosed clinically. Right heart catheterization confirmed the presence of severe pulmonary stenosis.

Surgical treatment was undertaken with cardiopulmonary bypass. An infundibular stenosis from a fibrous ring and muscular hypertrophy was found in the right ventricle with a right ventricular pressure of 140 mm. Hg and a pulmonary artery pressure of 40 mm. Hg; the pulmonary valve was normal. The stenotic area was easily excised. A long narrow subvalvular stenosis was found in the left ventricle with a small ventricular

septal defect; left ventricular pressure was 160 mm. Hg. Death occurred from injury to the ventricular septum during attempted excision of the subvalvular stenosis.

Autopsy findings. The heart weighed 180 grams. Both right and left ventricles were enlarged, the right ventricular wall measuring 15 mm. in thickness. The pulmonary and aortic valves were normal. A fibrous stenotic area 1 cm. below the pulmonary valve had been surgically enlarged to about 8 mm. in diameter. A "tunnel-like" fibrous stenotic area 1 to 2 cm. below the aortic valve had been enlarged to about 5 mm. in diameter. There were 2 ventricular septal defects, a 5-mm. one above the area of stenosis, probably resulting from surgical trauma, and a 4-mm. one below the stenosis.

Surgical Considerations

A photograph of the heart in case 42 is shown in figure 6. The tunnel-like stenosis in the left ventricular outflow tract can be clearly seen. This type of long stenotic area was present in both patients in this group, whereas all of the 10 patients with isolated subvalvular stenosis had a narrow fibrous ring. The length of the stenotic area in these 2 patients considerably increased the surgical risk of injury to the ventricular septum when the stenosis was excised.

AORTIC STENOSIS WITH UNDERDEVELOPED LEFT VENTRICLE

Aortic stenosis in 3 patients (cases 44, 45 and 46, table 1) was only a part of a hypoplasia involving the whole left side of the heart.[12] Surgical procedures should be avoided whenever possible in patients with these extensive malformations. These 3 patients are briefly described below.

Case 44. Left ventricular-right atrial shunt. M. T., a 2-year-old girl, has been previously reported.[8] She had cardiac failure in infancy, and a diagnosis of aortic stenosis was made because of a harsh systolic murmur, a decreased aortic second sound, and findings of left ventricular hypertrophy on roentgenograms and electrocardiogram. Death resulted from an aortic valvulotomy attempted in 1956 by the transventricular approach. Autopsy showed a left ventricular-right atrial defect with aortic obstruction in the left ventricular outflow tract from a dense network of anomalous chordae tendinae associated with a cleft aortic leaflet of the mitral valve.

Case 45. Valvular aortic stenosis, mitral valve deformity, hypoplasia of left ventricle. M. C. (JHH813547), a 4-year-old Caucasian boy, was diagnosed as having aortic stenosis at 5 months of age. He had frequent respiratory infections,

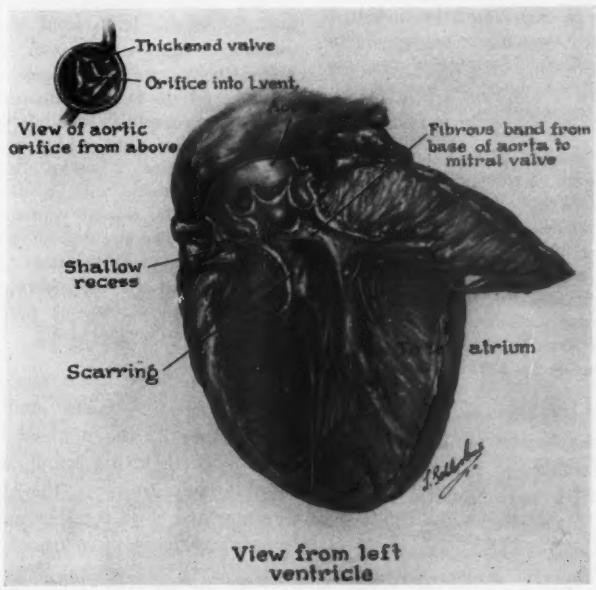

FIG. 6. Heart and aorta of case 42, table 1, showing a fibrous stenosis of the left ventricular outflow tract which was about 2 cm. in length.

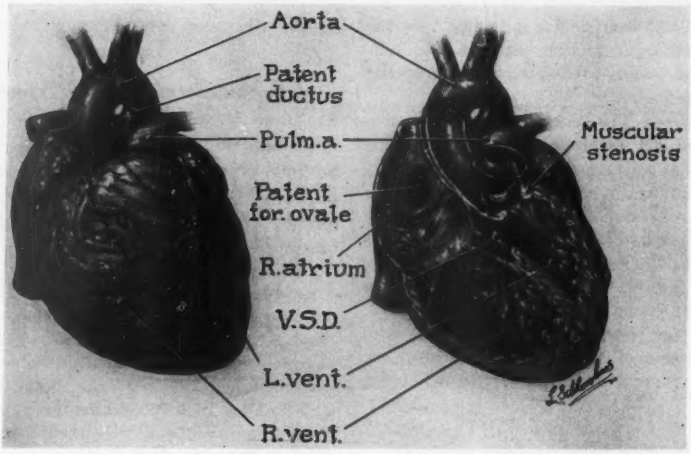

FIG. 7. Heart and aorta of case 46, table 1, showing multiple abnormalities in left side of heart. The aorta is hypoplastic, a subvalvular stenosis is present, the left ventricular cavity is small, and a large ventricular septal defect is present.

but no angina or syncope. There was a harsh systolic murmur and thrill maximal in the right second interspace and conducted over the precordium and into the neck. The second sound in the aortic area was absent. Blood pressure was 94/70 mm. Hg. Chest roentgenograms showed an enlarged left ventricle and marked enlargement of the left atrium. Electrocardiogram showed extreme left ventricular hypertrophy with ST depression and T-wave inversion; these changes had been present since the age of one year. Aortic valvulotomy was performed because of dyspnea, cardiac enlargement and severe left heart strain. He died 12 hours after operation.

Autopsy findings. The heart weighed 750 gm.; the right heart was normal. The aortic valve was bicuspid with thick nodular cusps, with a recent surgical incision in one commissure. The left ventricular musculature was greatly hypertrophied, measuring 19 mm. in thickness. The mitral valve was small with the leaflets thickened, deformed, shortened and fused with thickened and shortened chordae tendinae. The left atrium was dilated and hypertrophied with endocardial thickening.[7] The coronaries were normal.

Comment. The significant clinical findings in this patient were the marked left atrial enlargement, and the presence of a left ventricular "strain" pattern from an unusually early age that had showed little progression. The first findings suggested mitral valve disease and the second suggested severe myocardial disease. Little relief could be expected from aortic valvulotomy since the left ventricle itself was underdeveloped, and the outflow tract was probably obstructed by the grossly malformed mitral valve.

*Case 46. Aortic hypoplasia, subvalvular stenosis, ventricular septal defect.** S. McD., 3 weeks old, developed severe cardiac failure at 1 week of age. A soft, poorly localized systolic murmur was heard down the left sternal border; the second pulmonic sound was normal. Chest roentgenograms showed marked enlargement of both ventricles and increased pulmonary vascularity. Electrocardiogram showed left ventricular hypertrophy. The infant showed no response to therapy and died within 2 weeks. Autopsy showed a hypoplastic aorta with a subvalvular aortic stenosis (fig. 7). A large ventricular septal defect was present. The circumference of the pulmonary valve was about three times that of the aortic valve. There was a large patent ductus arteriosus supplying the descending aorta which was of approximately normal size.

Comment. Since aortic stenosis is known to cause congestive failure and left ventricular hypertrophy in the newborn, confusion might possibly occur with a complicated malformation of this kind. However, the absence of a good murmur and thrill together with the roentgenographic evidence of increased vascularity indi-

* We are indebted to Dr. Grimes of Baltimore for permission to publish this case.

cated that an uncomplicated aortic stenosis was not present.

DISCUSSION

It was encouraging that about 80 per cent of this group of 46 patients had either valvular or subvalvular stenosis because this type of stenosis can readily be corrected with a low operative risk with present surgical techniques.

The absence of any deaths in 22 patients operated upon for uncomplicated valvular stenosis indicates the safety of existing methods. The low incidence of aortic insufficiency is probably due to limiting the valvulotomy to fused commissures which are well developed. This limited valvulotomy has adequately relieved the obstruction as indicated by post-valvulotomy pressure gradients. Valvulotomy in the presence of thickened cusps may have a greater risk of insufficiency because of retraction and loss of mobility of the valve cusp.

Excision of subvalvular stenosis is associated with a greater hazard of injury to vital structures, but the risk is small with good visualization of the stenotic area as it is excised.

Further study is needed to determine the mechanism of obstruction in so-called "muscular" aortic stenosis. Cine-angiography is probably the most promising method of study for this problem.

The frequency of multiple anomalies in the very young indicates the need for caution in operative procedures in this group. The usual clinical picture of valvular and subvalvular stenosis has often not been seen in this group.

SUMMARY

The anatomical findings in a series of 46 patients with congenital aortic stenosis have been presented. In all of them the diagnosis was confirmed by open heart surgery or by autopsy.

One patient with supravalvular aortic stenosis died from a transventricular valvulotomy after progressive cardiac failure had followed bacterial endocarditis.

Of 27 patients with valvular stenosis, 3 had additional subvalvular stenosis, 2 had an unusually narrow valve ring, and 6 had thickened cusps. In 17 of the 27 the valve showed a typical pattern of complete "fusion" between the right and left coronary cusps and partial fusion in the area of the other two commissures. Of the 27 patients 24 underwent open heart surgery. There was one death in an infant who also had a coarctation, a patent ductus arteriosus, and intractable left ventricular failure. The remaining 23 cases have all done well although 5 of these have some aortic insufficiency. The risk of aortic insufficiency or incomplete relief of the stenosis was greater when the "typical" valvular stenosis was not present. Three patients, two of them infants, died before surgery could be attempted.

Subvalvular stenosis due to a fibrous ring 1 to 2 cm. below the aortic valve was present in 10 patients; 9 underwent open heart surgery with 2 deaths. The anatomical relations of the fibrous ring and the hazards of its removal are discussed and illustrated. A 7-year-old boy with some atypical findings died without operation in his first attack of pulmonary edema. Subvalvular obstruction, presumably due to muscular hypertrophy, was diagnosed in 3 patients in 2 of whom no anatomical obstruction could be found at operation. All survived and one has shown striking regression of her left ventricular hypertrophy. The diagnostic criteria are discussed.

Combined aortic and pulmonic stenosis occurred in two patients; both died after attempted correction. The infundibular stenosis in the combined type was more diffuse than that found as an isolated subvalvular stenosis.

Three cases are described in which aortic stenosis formed only part of an underdeveloped left side of the heart and in whom no relief could be obtained or hoped for by aortic valvulotomy.

The surgical results are best and the difficulties least in the patients with a typical pattern of valvular stenosis. Increased difficulties and hazards attend the more complicated anatomical lesions.

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REFERENCES

1. Abbott, M. E.: *Atlas of Congenital Cardiac Disease*. The American Heart Association, Inc., New York, 1954.
2. Bercu, B. A., Dietterт, G. A., Danforth, W. H., Pund, E. E., Jr., Ahlvin, R. C., and Belliveau, R. R.: Pseudo-aortic stenosis produced by ventricular hypertrophy. Am. J. Med., *25:* 814, 1958.
3. Brock, R.: Functional obstruction of the left ventricle. Guy's Hosp. Rep., *106:* 221, 1957.
4. Brock, R., and Fleming, P. R.: Aortic sub-

valvular stenosis. Guy's Hosp. Rep., *105:* 391, 1956.

5. Campbell, M., and Kauntze, R.: Congenital aortic valvular stenosis. Brit. Heart J., *15:* 179, 1953.
6. Denie, J. J., and Verheugt, A. P.: Supravalvular aortic stenosis. Circulation, *18:* 902, 1958.
7. DuShane, J. W., and Edwards, J. E.: Cardiac clinics: congenital aortic stenosis in association with endocardial sclerosis of the left ventricle. Proc. Staff Meet. Mayo Clin., *29:* 102, 1954.
8. Ferencz, C.: Atrio-ventricular defect of membranous septum. Bull. Johns Hopkins Hosp., *100:* 209, 1957.
9. Heath, D., Edwards, J. E., and Smith, L. A.: The rheologic significance of medial necrosis and dissecting aneurysm of the ascending aorta in association with calcific aortic stenosis. Proc. Staff Meet. Mayo Clin., *33:* 228, 1958.
10. Marquis, R. M., and Logan, A.: Congenital aortic stenosis and its surgical treatment. Brit. Heart J., *17:* 373, 1955.
11. Morrow, A. G., and Braunwald, E.: Functional aortic stenosis. Circulation, *20:* 181, 1959.
12. Morrow, A. G., Sharp, E. H., and Braunwald, E.: Congenital aortic stenosis. Circulation, *18:* 1091, 1958.
13. Nadas, A. S.: *Pediatric Cardiology*. W. B. Saunders Company, Philadelphia, 1957.
14. Sissman, N. J., Neill, C. A., Spencer, F. C., and Taussig, H. B.: Congenital aortic stenosis. Circulation, *19:* 458, 1959.
15. Smith, D. E., and Matthews, M. B.: Aortic valvular stenosis with coarctation of aorta with special reference to development of aortic stenosis upon congenital bicuspid valves. Brit. Heart J., *17:* 198, 1955.
16. Spencer, F. C., Neill, C. A., and Bahnson, H. T.: The treatment of congenital aortic stenosis with valvotomy during cardiopulmonary bypass. Surgery, *44:* 109, 1958.
17. Wood, P.: Aortic stenosis. Am. J. Cardiol., *1:* 553, 1958.

CORONARY ENDARTERECTOMY*

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Endarterectomy has become an accepted and established method of therapy in the management of a variety of clinical conditions which are the result of atherosclerotic arterial occlusion. Removal of lesions by this method from the aorta, iliac, and femoral vessels has been shown to be highly beneficial in the relief of vascular obstruction. Recently the employment of endarterectomy on vessels of smaller caliber including the internal carotid, vertebral and superior mesenteric arteries has also been successful. These encouraging results have stimulated an interest in the use of this procedure in the management of myocardial ischemia produced by coronary atherosclerosis. The present communication concerns a group of clinical observations recently made on several patients with angina pectoris in whom coronary endarterectomy was performed.

REPORT OF CASES AND OPERATIVE TECHNIQUE

Case 1. A 41-year-old engineer was admitted to The Johns Hopkins Hospital with the complaint of severe chest pain typical of angina pectoris. The family history revealed that the father had angina and died after a cerebral vascular accident. The mother is living and has hypertensive cardiovascular disease. There was nothing significant in the past history. The present illness began 7 years before admission with the onset of sudden severe chest pain and prostration. The patient was admitted to a hospital where an electrocardiogram was thought to show evidence of myocardial infarction. He was placed on bed rest for 2 months and was discharged asymptomatic. Two years later the onset of chest pain was noted on mild exertion. This gradually became more severe and could be induced by walking 50 feet. It was characteristically relieved by sublingual nitroglycerin. The pain ultimately forced him to cease work and remain essentially at rest.

On admission the physical examination was not remarkable. The blood pressure was 120/80, and all peripheral pulses were palpable. Laboratory studies revealed a serum cholesterol of 295 mg. per cent. The electrocardiogram at rest was normal, but after exercise the tracing showed ventricular extrasystoles and slight depression of ST 1 and marked depression of ST 2, ST 3, and T 4 regarded as evidence of myocardial ischemia. A coronary arteriogram was performed and showed good filling of the left coronary artery and its anterior descending and circumflex branches. The right coronary artery was visualized for a distance of approximately 1 cm. and a single small branch was patent. There was no filling of the right coronary artery distally, and it was concluded that there was a complete block at this site. The arteriogram is shown in figure 1, and comparison is made with an illustration of a right coronary artery in a normal patient.

On February 12, 1959, a bilateral anterior thoracotomy with sternal transection was performed using Pentothal and nitrous oxide anesthesia. Both pleural cavities were entered, and the pericardium was opened widely. The left main, anterior descending, and circumflex coronary arteries were each firm but compressible. Palpation of the right coronary artery revealed it to be enlarged and quite hard. It was dissected free of the surrounding fat in the auriculoventricular groove from its aortic origin to the lateral border of the right atrial appendage (fig. 2). It was then occluded with an arterial clamp for 5 min. During this time no change occurred in the systemic arterial pressure, the appearance or action of the heart, or in the electrocardiogram. It was concluded that the right coronary artery was probably totally occluded, and a longitudinal incision was made approximately 2 cm. from the origin (fig. 3*A*). Upon incising the adventitia and entry into the muscular layer a good cleavage plane was developed. With the coronary arterial dissector the thrombus was freed throughout its circumference, and the dissector was directed toward the aorta (fig. 3*B*). The thrombus was doubly ligated and divided (fig. 4*A*). The proximal ligature was passed through an arterial stripper and the thrombus drawn tightly as the stripper was advanced in the plane of cleavage (fig. 4*B*, *C*, and *D*). As the proximal end of the thrombus was reached, a jet of blood escaped through the arteriotomy (fig. 4*E*). The thrombus was removed and the artery was occluded proximally. A similar

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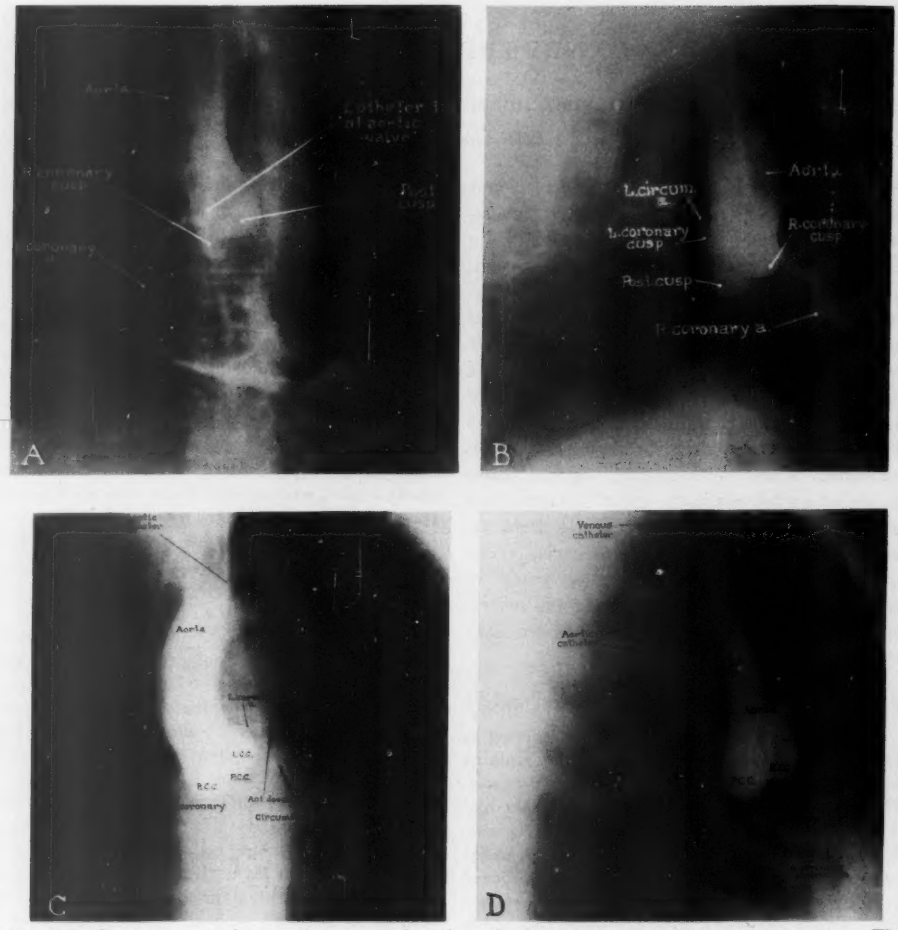

FIG. 1*A*. Coronary arteriogram in a normal patient demonstrating the right coronary artery. The catheter tip is near the orifice of the right coronary artery. The right coronary cusp and entire length of the right coronary artery are shown. *B*. Lateral view of arteriogram shown in *A*. *C*. Coronary arteriogram of case 1 showing good filling of the aorta and moderately good filling of the left coronary artery with its anterior descending and circumflex branches. The lumen of the right coronary artery is almost totally occluded near its origin. *D*. Lateral film showing small caliber right coronary artery with patent first branch. The remainder of the right coronary artery is totally occluded and contrasts with the normal vessel illustrated in *A* and *B*.

procedure was performed distally as shown in figure 5*A*. With the removal of the distal thrombus an appreciable quantity of back-bleeding occurred. The total length of the specimen was 7 cm. and a photograph is shown in figure 6*A*. An x-ray showed the presence of calcium in the thrombus (fig. 6*B*), and histologic sections demonstrated an area of total occlusion (fig. 6*C*). The arteriotomy was closed with a continuous suture of 6-0 arterial silk with a BV-1 needle* and the occluding clamp near the aortic orifice was removed. The chest was closed with catheter drainage of both pleural cavities. The patient recovered without event from operation. The postoperative electrocardiogram showed minimal ischemic changes. He has since returned to full-time work as an engineer with considerable symptomatic improvement.

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Case 9. A 49-year-old man was referred to The Johns Hopkins Hospital with the diagnosis of

FIG. 2. Illustration of exposure obtained through a median sternotomy. The pericardium is opened and the right main coronary artery dissected near its origin from the aorta.

angina pectoris due to coronary arterial insufficiency. The family and past histories were noncontributory. The present illness began 2 years before admission with the onset of substernal pain which was characteristically relieved by nitroglycerin. An exercise test performed at the time showed electrocardiographic evidence of myocardial ischemia. The pain became progressively worse and he found it necessary to stop work.

On examination the blood pressure was 140/80. The remainder of the findings were within normal limits except for diminished pulsations in all the arteries of the lower extremities. The serum cholesterol was 365 mg. per cent and total lipids 897 mg. per cent. The electrocardiographic exercise test was positive. A coronary arteriogram showed satisfactory visualization of the left coronary artery and its branches with no filling of the right coronary artery.

On May 14, 1959, a median sternotomy was performed, and the vessels were palpated. The left coronary and its branches were thickened; the right was hard and uncompressible. The latter was dissected and occluded for 5 min. without effect on the systemic pressure or electrocardiogram. The right coronary artery was then opened and a thrombus, 5 cm. in length, with total occlusion of the lumen was removed (fig. 7*A* and *B*). The technique employed was essentially the same as that in the first patient. It was well tolerated, and the postoperative recovery was

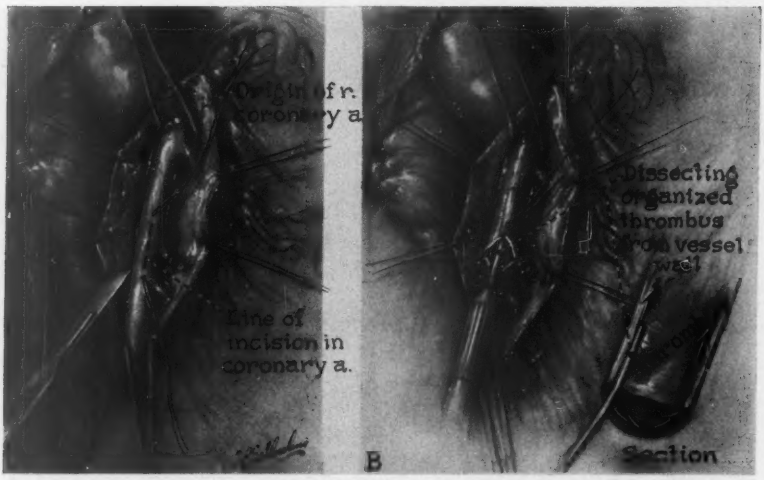


FIG. 3A. The right main coronary artery has been exposed from its origin to a point several centimeters distally. Two stay sutures are placed preparatory to the arteriotomy. *B.* A short longitudinal incision is made, and the coronary arterial dissector is employed. The instruments used are those designed by Longmire and Cannon.

unremarkable. The electrocardiogram was normal at rest and after exercise showed ST segment depression. Since discharge the patient has noted a marked reduction in the previous anginal pain and has resumed work.

Case 3. A 43-year-old man was referred with a diagnosis of angina pectoris. The family and past histories were noncontributory. Fifteen months before admission the patient had an episode of substernal pain which radiated across the left anterior chest. An electrocardiogram after exercise was stated to have shown evidence of myocardial insufficiency, and nitroglycerin was found to relieve the pain. The attacks became more frequent, and in April 1958 bilateral ligation of the internal mammary arteries was performed. This did not bring relief, and the use of nitroglycerin was continued in large amounts. Finally he found it necessary to retire completely from work. At the time of admission an attack could be precipitated by walking across the room.

The physical examination was essentially negative. The blood pressure was 125/70, and the laboratory findings included a serum cholesterol of 175 mg. per cent and total lipids of 720 mg. per cent. The electrocardiogram showed T-wave changes indicative of coronary arterial insufficiency. A coronary arteriogram was performed which demonstrated a block in the left main and circumflex coronary arteries. The right coronary artery filled but was narrowed at its origin.

On September 11, 1959, a left posterolateral thoracotomy was performed. The chest was entered through the bed of the resected 5th rib, and the pericardium was opened widely. The left main coronary artery was quite hard, and the process was found to extend for approximately 2 cm. into the anterior descending and circumflex branches. The main vessel was dissected free of the surrounding tissues, and an occluding clamp was applied for 5 min. No changes occurred in the systemic arterial pressure, heart action or electrocardiogram. The circumflex artery was opened first and an attempt made to dissect the thrombus. It was not possible to withdraw the rather large occluding lesion present in the left main coronary artery through the opening in the circumflex branch, and the wall of the latter was torn in an effort to remove it in this manner. At this point the left main coronary artery was incised, and using the arterial dissector, atheromatous plaques were removed from the origin of the vessel including its circumflex and anterior descending branches. The involvement in these vessels was extensive with complete occlusion of the left main coronary artery. It was not possible to remove the obstruction totally, and although the procedure was well tolerated at the time, the patient developed ventricular tachycardia followed by irreversible ventricular fibrillation later on the day of operation. Postmortem examination of the left coronary artery and the anterior descending and circumflex branches showed residual plaques and fresh thrombus. The right coronary artery showed diffuse atherosclerosis with a patent lumen.

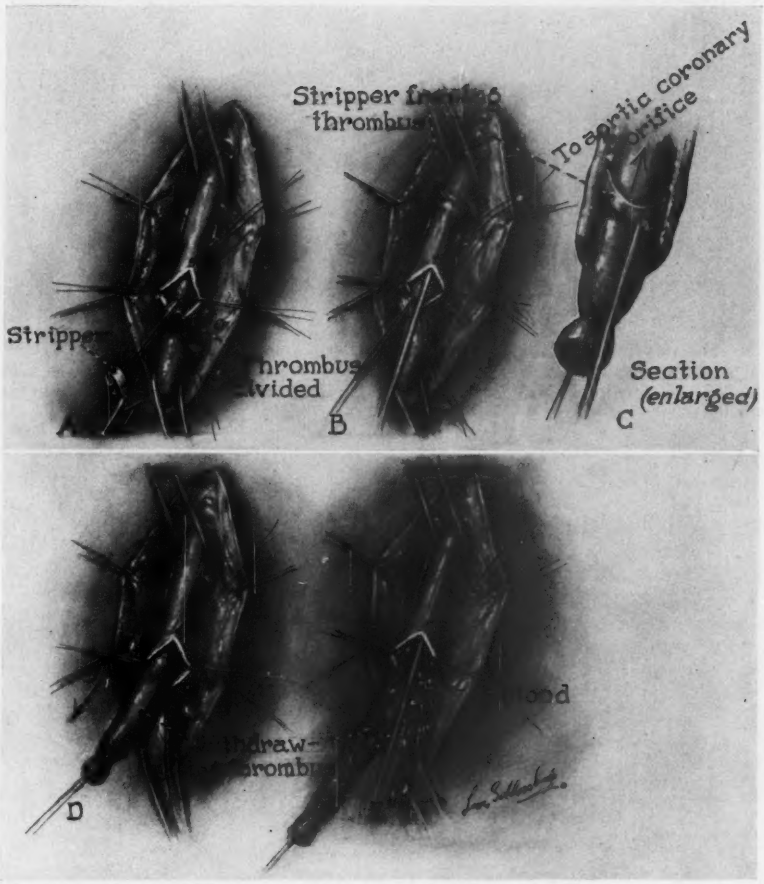


FIG. 4A. The thrombus is divided and a ligature is placed on both ends. *B*. The ligature is pulled through the orifice of the coronary stripper, and the stripper is advanced toward the aorta freeing the thrombus from the muscularis of the coronary artery. *C*. Illustration of coronary stripper employed for separation of the thrombus from the arterial wall. *D*. After complete separation of the thrombus from the arterial wall, traction is applied to the ligature, and the thrombus is removed from the artery. *E*. Following removal of the thrombus, a sudden jet of blood escapes from the artery.

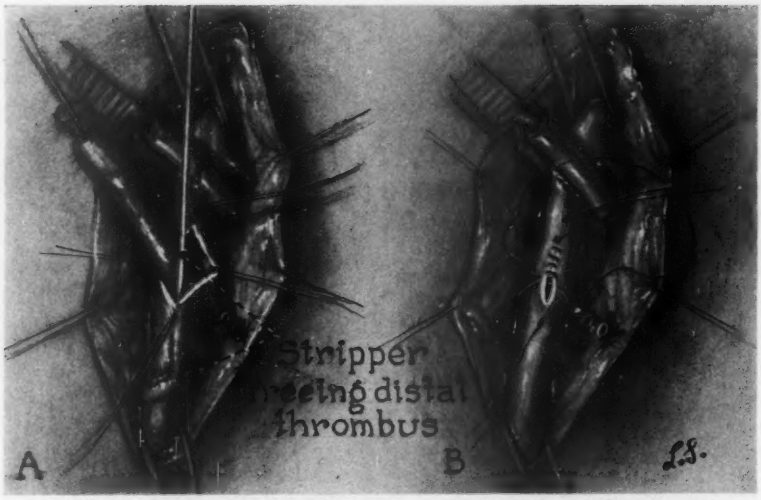


FIG. 5*A*. A stripper is applied to the distal thrombus which is dissected free from the arterial wall. During this time the proximal artery is occluded with an arterial clamp. *B*. The arteriotomy is carefully closed with 6-0 arterial silk.

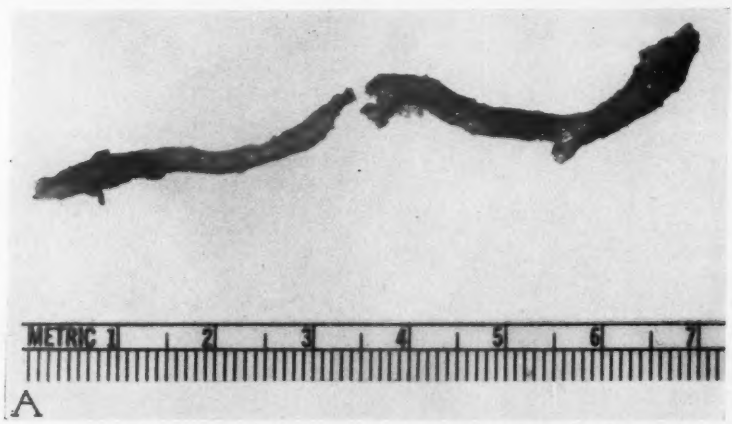


FIG. 6*A*. Photograph of gross specimen removed at operation in case 1

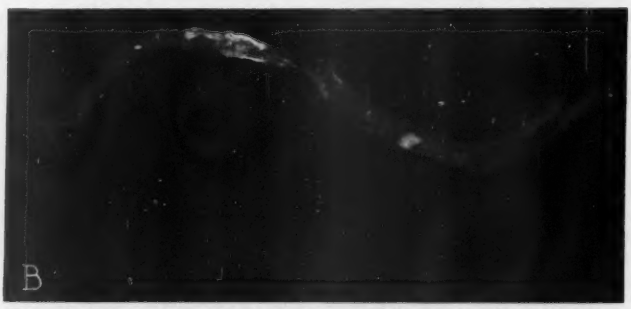
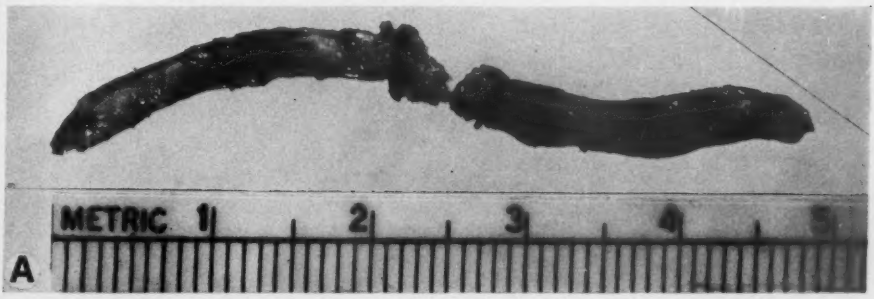


FIG. 6*B*. Roentgenogram of specimen showing areas of calcification

FIG. 6C. Photomicrograph (× 40) of endarterectomy specimen of case 1 showing complete occlusion.



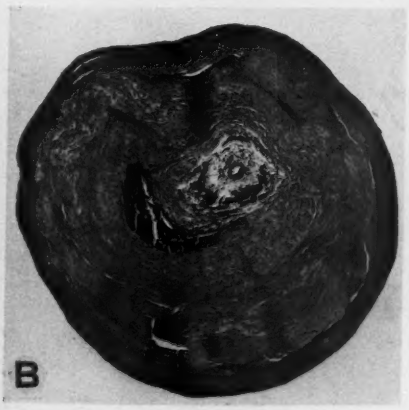


FIG. 7A. Photograph of gross specimen removed at operation in case 2

FIG. 7B. Photomicrograph (× 30) of the organized thrombus shown in figure 7A.

DISCUSSION

The feasibility of direct endarterectomy for the relief of coronary arterial occlusion is dependent upon several factors. These include (1) the anatomical distribution of coronary atherosclerosis, (2) the status of the arterial vascular bed distal to the occlusion, (3) the technical problem of removal of lesions in the coronary arteries and satisfactory reconstruction, and (4) the predisposition to thrombosis in small arteries after endarterectomy. Although it is not possible to answer these points completely, data are presently available concerning each and may be considered in a discussion of the problem.

Distribution of coronary atherosclerosis. Several groups of investigators have studied large numbers of hearts at postmortem examination, and it has shown that in most instances coronary atherosclerosis is a part of generalized arterial disease with involvement of multiple vessels throughout the body. Despite this fact it is well recognized that a considerable degree of atherosclerosis may be present throughout the body and yet well tolerated. When serious difficulty occurs, it is usually found to be the result of marked narrowing or complete obstruction of one or more important arteries. Experience has shown that removal of such an occlusion often may provide relief for a prolonged period. Pathologic studies concerning the distribution of atherosclerosis in the *coronary* arteries indicate that the chief involvement is in the larger, subepicardial vessels while the deeper and smaller intramyocardial vessels are essentially free of disease. In a thorough gross and microscopic study of 400 hearts at postmortem examination, Schlesinger and Zoll[13] concluded that "most zones of occlusion of the coronary arteries are less than 5 mm. in length." They further observed that "the majority of coronary occlusions are found within 3 cm. of the mouths of these vessels." These and other similar studies[1] confirm the fact that in many instances coronary arterial occlusion is segmental in distribution and occurs near the origin of the vessels.

The arterial bed distal to the site of occlusion. One of the basic principles which determines the success of any endarterectomy is the degree of patency of the vessels distal to the obstruction. The importance of this factor has been observed particularly in the lower extremities where the amount of backbleeding has been shown to be of great significance in an estimation of the prognosis. This principle is of added importance in the coronary arteries since these vessels have been termed "end arteries" due to the reduced number of interarterial collateral vessels normally present in the myocardium. Gregg[7] and Gregg and associates[8] have made a significant contribution to this problem in a study of the experimental hemodynamics after chronic occlusion of a major coronary artery. Both back pressure and backflow in the distal portion of the occluded artery were found to be increased greatly after a period of chronic ligation. These studies show that collateral channels develop and conduct appreciable quantities of blood. Postmortem observations in human hearts have indicated that intercoronary anastomoses greater than 40 μ in diameter are not found in normal hearts, whereas collateral vessels measuring 40 to 200 μ in diameter regularly develop in the presence of coronary arterial obstruction.[3] These collateral vessels supply blood to the coronary circulation distal to the point of occlusion. Further evidence of the patency of the distal coronary bed has been supplied by recent perfusion studies in our laboratory in hearts obtained at autopsy from patients with myocardial infarction. After endarterectomy a marked increase was found in the volume of fluid which could be perfused through the coronary arteries.[10] Each of these observations tends to support the view that coronary arteries distal to an obstruction are often patent.

The technical problem of coronary endarterectomy. From the operative viewpoint there is little doubt that endarterectomy is most easily accomplished in vessels of moderate or large size. The initial clinical procedures were performed in vessels of this caliber, but with the passage of time smaller arteries have been attacked and successful results reported. Included in this group are endarterectomies of the internal carotid,[6] vertebral,[5] and superior mesenteric arteries.[14] Widespread interest in the surgical management of occlusive coronary artery disease has led to a consideration of its use for this disease, and Bailey and associates[2] were the first to report a successful coronary endarterectomy. Cannon and co-workers[4] and Longmire and associates[9] have recently presented their results of operation in 9 patients. The operative technique employed in the present patients is essentially the one which they developed.

Predisposition of small arteries to thrombosis after endarterectomy. One of the problems which has been encountered in the direct removal of occluding lesions of small arteries has been the predisposition to postoperative thrombosis. The problem is an important one, and further clinical studies are necessary before the final answer to this question is available. In a group of experiments in our laboratory, indirect evidence was obtained on this point. A long segment of the left carotid artery, with the proximal end intact at the brachiocephalic artery, was drawn into a tunnel in the left ventricular myocardium. The branches were allowed to remain open, and the vessel was fixed in place at the cardiac apex by a suture. Under these circumstances the carotid implants remained patent in most of the hearts. However, similar implants of the carotid and femoral arteries into the sternomastoid muscle, liver, and spleen uniformly resulted in thrombosis.[11] It is possible that the rhythmic contraction of the heart retards the development of thrombosis. In another experimental study, endarterectomy with removal of the intima and a portion of the muscular layer was performed on the femoral arteries of the dog.[12] These vessels were 3.0 to 4.0 mm. in diameter and comparable in size to coronary arteries found in the human. Long term patency of the lumen was demonstrated in 90 per cent of the animals by arteriogram and histologic examination. It is recognized that these studies were done on normal vessels, whereas similar procedures on humans are performed in association with atherosclerosis. Current studies are in progress to determine the effect of experimental canine atherosclerosis on the results of experimental endarterectomy in small vessels.

A summary of the several factors considered to be important in the rationale of coronary endarterectomy indicate that the anatomical localization of lesions, status of the distal arterial vascular bed, and feasibility of technical removal are each favorable in *selected* patients with coronary atherosclerosis. At present it appears that the patient with severe angina pectoris *without* a proved history of myocardial infarction is the most suitable candidate for the procedure. In our experience coronary arteriograms obtained preoperatively have been of considerable aid in the establishment of an accurate anatomical diagnosis and localization of the lesion. A group of over 30 such studies has been done with no significant morbidity and no mortality.

While experimental and clinical evidence is available which supports the rationale of coronary endarterectomy, the fact remains that in many instances coronary atherosclerosis is an extensive disease and is probably beyond the scope of an excisional therapy. At the present this method should be considered to be in a stage of evaluation, and conclusions regarding its role in the management of coronary atherosclerosis are dependent upon further observation and study.

SUMMARY

The physiologic and pathologic features of coronary atherosclerosis which are pertinent to the rationale of coronary endarterectomy in the management of myocardial ischemia have been reviewed. Emphasis has been placed upon the value of accurate preoperative localization of the site of occlusion by arteriography. Coronary endarterectomy has been performed under direct vision for severe angina pectoris with a successful result in two of three patients in whom it has been employed.

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REFERENCES

1. Absolon, K. B., Aust, J. B., Varco, R. L., and Lillehei, C. W.: Surgical treatment of occlusive coronary artery disease by endarterectomy or anastomotic replacement. Surg. Gynec. & Obst., *103:* 180, 1956.
2. Bailey, C. P., May, A., and Lemmon, W. M.: Survival after coronary endarterectomy in man. J. A. M. A., *164:* 641, 1957.
3. Blumgart, H. L., Schlesinger, M. J., and Davis, D.: Studies on the relation of clinical manifestations of angina pectoris, coronary thrombosis and myocardial infarction to the pathologic findings with particular reference to significance of collateral circulation. Am. Heart J., *19:* 1, 1940.
4. Cannon, J. A., Longmire, W. P., Jr., and Kattus, A. A.: Consideration of the rationale and technique of coronary endarterectomy for angina pectoris. Surgery, *46:* 197, 1959.
5. Cate, W. R., Jr., and Scott, H. W., Jr.: Cerebral ischemia of central origin: relief by subclavian-vertebral artery thromboendarterectomy. Surgery, *45:* 19, 1959.
6. DeBakey, M. E., Crawford, E. S., Cooley, D. A., and Morris, G. C., Jr.: Surgical considerations of occlusive disease of the abdominal aorta and iliac and femoral arteries: analysis of 803 cases. Ann. Surg., *148:* 306, 1958.

7. GREGG, D. E.: *Coronary Circulation in Health and Disease*. Lea & Febiger, Philadelphia, 1950.
8. GREGG, D. E., THORNTON, J. J., AND MAUTZ, F. R.: The magnitude, adequacy and source of the collateral blood flow and pressure in chronically occluded coronary arteries. Am. J. Physiol., *127:* 161, 1939.
9. LONGMIRE, W. P., JR., CANNON, J. A., AND KATTUS, A. A.: Direct-vision coronary endarterectomy for angina pectoris. New England J. Med., *259:* 993, 1958.
10. SABISTON, D. C., JR., AND BLALOCK, A.: Physiologic and anatomic determinants of coronary blood flow and their relationship to myocardial revascularization. Surgery, *44:* 406, 1958.
11. SABISTON, D. C., JR., FAUTEUX, J. P., AND BLALOCK, A.: An experimental study of the fate of arterial implants in the left ventricular myocardium with a comparison of similar implants in other organs. Ann. Surg., *145:* 927, 1957.
12. SABISTON, D. C., JR., SMITH, G. W., AND TALBERT, J. L.: Evaluation of experimental endarterectomy in vessels of various size. Surg. Gynec. & Obst., in press.
13. SCHLESINGER, M. J., AND ZOLL, P. M.: Incidence and localization of coronary artery occlusions. Arch. Path., *32:* 178, 1941.
14. SHAW, R. S., AND MAYNARD, E. P.: Acute and chronic thrombosis of the mesenteric arteries associated with malabsorption. New England J. Med., *258:* 874, 1958.

ADDENDUM

Since preparation of this manuscript coronary endarterectomy has been successfully performed in two additional patients.

EXPERIENCES WITH OPEN HEART SURGERY DURING CARDIOPULMONARY BYPASS IN 270 CASES*

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Between March 1956 and November 1959, 270 open cardiac operations have been performed at The Johns Hopkins Hospital with cardiopulmonary bypass. This report describes the method by which the pump-oxygenator is presently used and the experiences responsible for our current ideas about intracardiac surgery. It concerns only work done with cardiopulmonary bypass. The other portion of our intracardiac work has recently been reported,[6] that related to the use of hypothermia and caval occlusion which we utilize for most patients with atrial septal defect and some with isolated pulmonary stenosis.

THE HEART-LUNG MACHINE

The Gaertner-Kay modification of the Gibbon screen oxygenator has been the apparatus used in all but the first 27 cases, the DeWall bubble oxygenator being used initially. Kay and Gaertner[4] described two principal modifications of the Gibbon machine which uses the vertical stainless steel screen as an oxygenating surface. These changes were (1) a reduction in the height of the screen and (2) the use of manual instead of automatic control of the blood pumps. A simplified circuit was also used. We believe the concept of the shorter screen remains valid as 85 per cent of oxygenation in the vertical screen oxygenator occurs in the first 25 cm. of screen height, as observed by Kay and Gaertner. On the other hand, many of the modifications initially introduced with a view to economy and simplicity have been replaced by equipment which represents a return to the principles initially established by Gibbon. The latest modifications include automatic maintenance of a constant volume of blood in the machine, venous inflow being accurately balanced by arterial return to the patient, and automatic return of blood scavenged from the heart and pericardium during the cardiopulmonary bypass by an additional DeBakey pump (fig. 1).†

A sliding mechanical filmer is used which abolishes the need for filling the oxygenator with saline and the accompanying dilution of the priming blood. Oxygenators with 8 and 20 screens are interchangeable. When the smaller oxygenator is used, less blood is required to prime the machine, and at the same time, the automatic control becomes more sensitive. Venous inflow to the machine is with gravity drainage through ½-in. internal diameter (I.D.) tubing to a level 60 cm. below the usual right atrial position. Blood is scavenged from the heart and pericardium with a similar drop in level, the siphon being initiated with suction regulated to a maximum of 22 mm. Hg. The apparatus can be filled and the screens filmed with 2900 ml. of blood for the 20-screen oxygenator and 2000 ml. for the 8-screen machine. After filming of the screens, 200 ml. can be returned to the reservoir for transfusion during the bypass. We have tried to make as small as possible the priming volume of the machine, but a much more important consideration in saving blood is the adequacy of the scavenging system for removal of blood from the heart and adjacent areas in the operative field. It is false economy to limit rigorously the priming volume of the machine and then discard many hundreds of milliliters of blood at the time of the bypass because of an inadequate scavenging system. Three aspirating tubes are available and capable of removing 3 to 4 L. of blood per min. from the operative field.

The apparatus as presently employed is capable of adding a maximum of about 9 ml. of oxygen per screen, or 180 ml. for the 20-screen oxygenator. Unless this capacity is exceeded arterial oxygen saturations above 92 per cent are regularly obtained. With large patients on bypass with our present oxygenator arterial saturation has fallen as low as 78 per cent without

*From the Department of Surgery, The Johns Hopkins Hospital and University, Baltimore, Maryland; aided by Grant H-1326 from the National Heart Institute, U. S. Public Health Service.

†The pump-oxygenator was built by John F. Edwards.

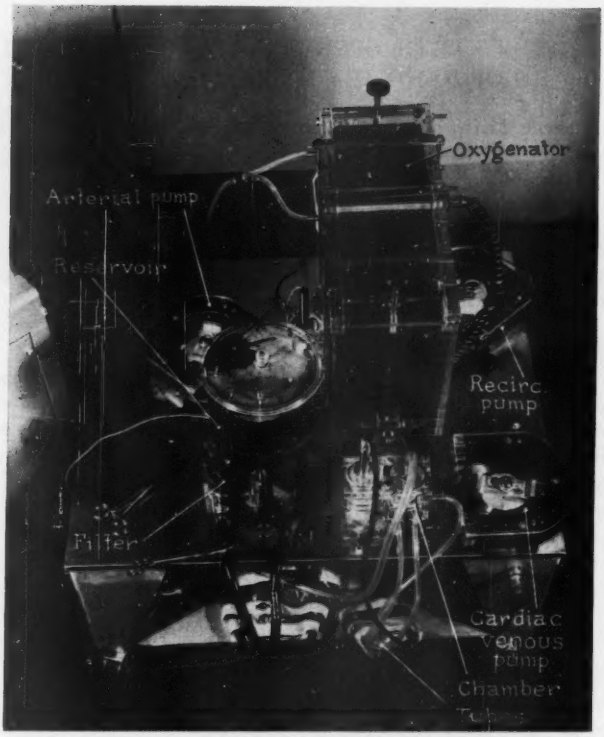

FIG. 1. Pump-oxygenator in current use. Electrical controls of the pumps are housed in a separate movable console.

detriment. With earlier smaller and less efficient models arterial saturations as low as 60 to 70 per cent occurred without evidence of embarrassment to the patient provided adequate blood flow was supplied. As arterial and venous saturations fall the oxygenator becomes more efficient and more oxygen can be added. Such low saturations are often seen in adults with the tetralogy of Fallot when bypass is first started since the mixed venous saturation and level of oxygenation throughout the body may be extremely low; as the bypass proceeds, oxygenation improves with elevation of venous saturation and with it the arterial saturation. The DeBakey pumps will handle up to 6 L. per min., although the need for flow this large has not been evident in our experience.

Adequacy of mechanical respiration and blood flow can be judged from blood pH values as shown in figures 2 and 3. Hyperventilation before the bypass results in alkalosis in almost all instances, but the pH returns toward a more normal range during the bypass. In the absence of subsequent cardiac or respiratory insufficiency acidosis has not occurred postoperatively. Ventilation of the oxygenator is with 15 L. per min. of humidified 2.5 per cent carbon dioxide in oxygen at approximately 37°C.

Free plasma hemoglobin has not risen alarmingly even in the adult tetralogy with bypass exceeding an hour and during much of which more than half the pump output may be aspirated through the scavenging suckers. Levels observed in the last 40 cases are shown in figure 4. Analyses were made on a Beckman model DU spectrophotometer and calibrated from known standards. Some pigment, possibly from hemolysis of sampling, is normally present as the average control value before bypass in this group was 55 mg. per cent. Admittedly these observations do not accurately quantitate but only reflect hemolysis caused by the machine as the patient continues to remove free hemoglobin from the blood, but levels obtained are well below a dangerous range.

After use the disassembled parts are washed

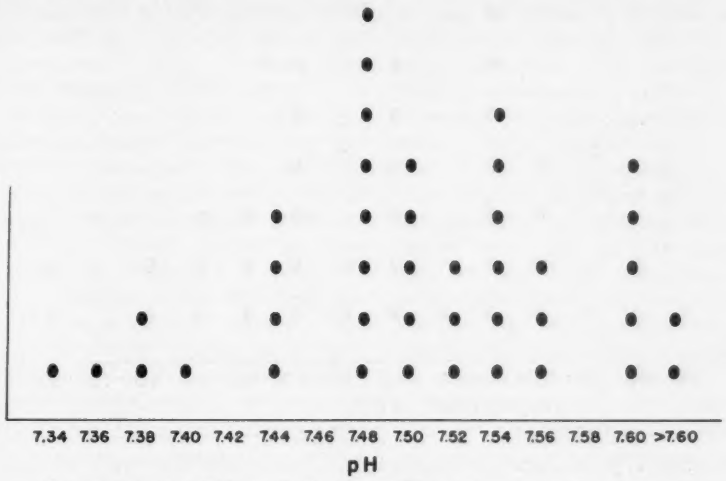

FIG. 2. Arterial pH from the last 40 patients taken just before bypass

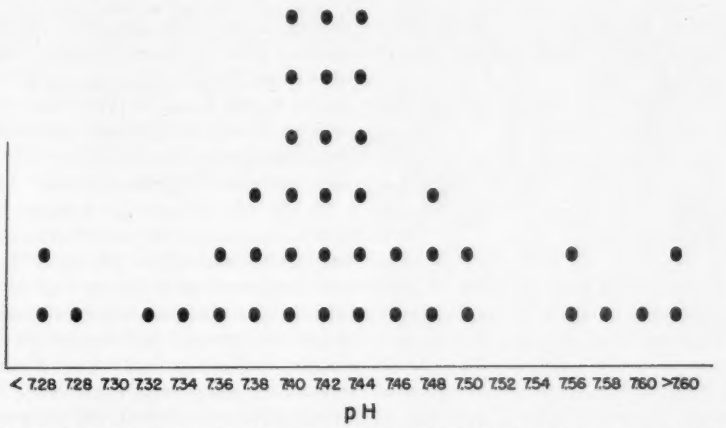

FIG. 3. Arterial pH at end of bypass or lowest obtained after bypass was started

with water and a detergent, soaked for 30 min. in 20 per cent solution of sodium hydroxide, thoroughly rinsed with tap water, dried and assembled. Absolute and reliable sterilization has been achieved by exposure of the assembled equipment in an atmosphere of ethylene oxide for 10 hr.[5]

CONDUCT OF THE BYPASS

Aortic and inferior vena caval pressures are monitored throughout the operation and postoperative period from catheters inserted percutaneously in the femoral vessels. Electrocardiogram is displayed on an oscilloscope, this being closely watched during intracardiac stitching in critical areas. Light anesthesia is given with nitrous oxide, succinylcholine, Pentothal or Fluothane. Active hyperventilation with resulting mild alkalosis augments the effect of anesthesia. The median sternotomy has given good exposure for most procedures, but the right anterolateral thoracotomy is used for atrial septal defects or anomalies of the venous return and for exposure of the mitral valve. In order to follow blood loss closely when a sternotomy is used, we attempt to avoid entry into the pleural cavity until completion of the procedure at which time a pericardial window is opened into the right pleural space and tube drainage used. In a few instances we have not opened the pleura

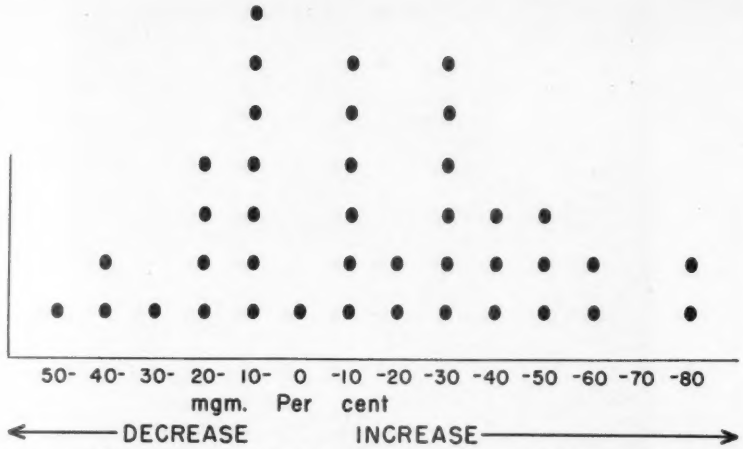

FIG. 4. Increment of plasma hemoglobin during bypass. In some cases there was a decrement from the pre-bypass value.

and drained only the pericardium; when this is done, one must carefully watch for evidence of cardiac tamponade.

Venous cannulation was usually through the right atrial appendage with ¼-in. I.D. tubing into each vena cava. In small children 3/16-in. tubing has been used. When work is planned in the right atrium, cannulae are inserted through stab wounds adjacent to the cavae. With siphon and gravity drainage no difficulty has been encountered in removing large quantities of blood through this siphon and tubing arrangement. Arterial return has been through the common femoral artery in most instances, the external iliac in one or two infants, and the innominate in several infants. In many cases of tetralogy of Fallot in which a subclavian-pulmonary shunt had to be ligated, the artery used in the shunt was cannulated for arterial return. Arteries to the lower extremity were reconstructed after completion of the bypass.

Heparin is given in a dose of 3 mg. per kg. to the patient, and the pump is primed with blood drawn the morning of operation from matched donors to which has been added 20 mg. of heparin for each 500 ml. of blood. We have feared much more the dangers of too little heparin than too much as one can neutralize the drug with protamine at the completion of the bypass. On the other hand, if large-scale clotting occurs during the bypass, fibrinolysis with resulting depletion of fibrinogen may develop which is much more difficult to treat. For this reason in recent cases we have given additional heparin, 1 mg. per kg., after every 30 min. of bypass. At the completion of the bypass 6 mg. of protamine are given for each kg. of body weight, and if additional heparin has been given, protamine is given to match the last additional dose on a 2:1 basis.

By use of open gravity drainage of blood to the machine and automatic return to the femoral artery of this blood, we attempt to approximate the cardiac output before beginning bypass. This volume of blood flow ranges usually between 2 and 3 L. per m.^{2} of body surface area. When an abnormally high flow is present and if arterial pressure is adequate as might occur when blood is emptied from a large heart, the excess may be stored in a reservoir until completion of the bypass. Similarly, transfusions are given if an unusually low flow is present.

With a flow of this magnitude an important aid has been a venting catheter in the left atrium, usually placed through the atrial appendage and attached to the suction-siphon scavenging system.

Cardiac asystole induced by potassium was used in the first 140 cases, but this appeared to be injurious as manifest in slow myocardial recovery, postoperative cardiac failure, and actual necrosis of muscle at postmortem examination. The harmful effect of potassium has been amply demonstrated by others experimentally.[3] For this reason we have abandoned potassium-in-

duced arrest and in the last 130 cases most of the intracardiac work has been done without prolonged interruption of coronary flow. When vision is obscured by aortic insufficiency or by excessive coronary venous return, the aorta may be intermittently clamped for periods up to 5 min., followed by restoration of flow for 1 min. and subsequent reclamping if necessary. Shorter periods of aortic occlusion are used if the electrocardiogram shows excessive bradycardia, heart block or evidence of ischemia.

In closing ventricular septal defects and the ostium primum type of atrial defect our best results have been with insertion of a patch approximating the size of the opening. Teflon felt has proved most satisfactory, the interstices and loose structure being associated with less leakage through it and at the same time forming a good matrix for subsequent clotting and sealing. When the outflow tract of the right ventricle must be enlarged with a patch, a porotin of woven Teflon aortic prosthesis has been used.

POSTOPERATIVE CARE

In the operating room blood volume is restored as nearly as possible to the preoperative level by transfusion of fresh citrated blood. Our most valuable guide in doing this has been the use of radioactive-tagged red cells to measure blood volume.[10] Although the method is not infallible it is remarkably accurate in demonstrating losses and additions to circulating volume. In addition and as a confirmation small children are weighed before and after operation, and a close check is made of blood loss by aspiration or on sponges during the operation. The measurement of blood volume postoperatively has been helpful in demonstrating losses which are not otherwise evident. After several earlier experiences of water intoxication and retention, fluids have been restricted to 600 ml. the day of operation, 900 ml. the second day, and 1200 ml. per m.^{2} of body surface area on subsequent days, our experience in this regard confirming that of Sturtz and his associates.[9] Penicillin, streptomycin, and erythromycin are given for 7 to 10 days unless there is a good history of previous sensitivity reaction.

Vinyl catheters placed at the beginning of the procedure in the femoral artery and vein and others placed at the end of the operation in the pulmonary artery and frequently the left atrium are used for withdrawal of blood samples postoperatively. Cardiac output can be estimated by oxygen saturation of the mixed venous blood from the pulmonary artery and adequacy of pulmonary ventilation determined from the left atrial or femoral sample.[2] Venous and left atrial pressures have often been helpful in determining limits to which transfusion might be pushed in the presence of a failing myocardium or low cardiac output. The pH of the arterial blood is measured, and if this drops below about 7.3, sodium bicarbonate is given intravenously. Except for the early postoperative period when acidosis may be due to hypoventilation, a low pH almost invariably indicates a diminished cardiac output which in some instances cannot be altered. Regardless, correction of the acidity has seemed beneficial to cardiovascular as well as central nervous system function.

Some degree of cardiac failure has been frequently seen after procedures requiring a ventriculotomy, such as ventricular septal defect or tetralogy of Fallot. Digitalis is now given almost routinely to such patients after bypass is completed. Digitalis is not usually given before operation because of a higher incidence of arrhythmias during operation in fully digitalized patients and also because of some uncertainty about possible loss of an indeterminate amount of digitalis into the blood in the pump-oxygenator system during bypass. Vasopressors have been used for hypotension from cardiac failure if urinary secretion is seriously decreased and the blood volume is adequate.

The patient is kept in an atmosphere high in humidity and oxygen for several days. In rare instances of severe pulmonary hypertension or pre-existing respiratory embarrassment a tracheotomy has been done at the time of the thoracotomy. After operation we do not hesitate to perform a tracheotomy if secretions are profuse and cannot be raised, if respirations are significantly embarrassed, or if the arterial oxygen saturation falls without obvious cause. In many instances a respirator has been used temporarily, although in one patient this was used for 40 days.[7]

Heart block, a serious problem in our early experience, has occurred much less frequently. Since sutures are placed in the region of the bundle of His with the heart beating, a damaging suture can be noticed by the beat or electrocardiogram. Several sutures have been replaced

for this reason. Except for heart block appearing with profound, and often terminal, cardiac failure we have not had this complication in the last 100 cases, and in one patient with pre-existing block the block disappeared when the bypass was started. In the earlier cases in which heart block occurred, treatment included the use of atropine, Isuprel, and ephedrine, main reliance being upon an electrical pacemaker through a wire implanted at the time of operation. When there was any question about the cardiac rhythm at the end of operation, an electrode wire has been sutured to the myocardium.

Postoperative hemorrhage continues to be a problem of considerable magnitude. A defect in the clotting mechanism has not been demonstrable *in vitro* in these patients except for two early experiences. In spite of the fact that clotting functions measured in the laboratory are normal and in spite of meticulous hemostasis during the operation, bleeding has been greater than after other thoracotomies. Postoperative bleeding has been especially severe in some of the older patients with tetralogy of Fallot and a hematocrit in the 70 to 85 per cent range. Re-exploration is made when bleeding is sudden, massive, or particularly if there appears to be cardiac tamponade. Particularly for the latter reason it has been performed more frequently in our recent experience.

Some degree of fever is regularly seen although this is less frequent and severe than in earlier experience. Aspirin, chlorpromazine, and occasionally physical cooling are used to keep the rectal temperature below 102.6° and thus avoid increased metabolic demands. General body hypothermia around 90 to 93° has been used when there is evidence of an acute nervous system insult.[11]

Infection of the operative area with Staphylococcus has resulted in the death of three patients, one with a cardiac abscess about an implanted Teflon aortic cusp, and two with mediastinal infection. One of these two required an unsterile thoracotomy and cardiac massage on the second postoperative day, and the other patient had been on long term adrenal steroid treatment for heart block. Two other patients with gross mediastinal infection have survived with open drainage.

DISCUSSION OF CASES

A summary of the cases treated and results is presented in table 1. A true picture of the opera-

TABLE 1

	Last 70 Cases May to Nov. '59		Second 100 Cases June '58 to May '59		First 100 Cases Mar. '56 to June '58	
	No. of cases	Survival	No. of cases	Survival	No. of cases	Survival
		%		%		%
Aortic stenosis						
Congenital	7	100	12	67	17	94
Adult	7	100	7	14	1	0
Aortic insufficiency	1	100	1	0		
Ventricular septal defect	16	88	24	79	54	67
Tetralogy of Fallot	17	59	24	75	5	20
Mitral insufficiency	2	50	4	50	5	40
Mitral stenosis	2	100	4	100	1	100
Pulmonary stenosis						
Intact ventricular septum	6	100	5	100	3	33
Atrial septal defect						
Secundum	3	100	4	100	3	66
Anomalies of pulmonary veins	2	100	1	100	3	67
Primum	2	100	7	72	5	20
Aneurysm of aortic arch	2	50	5	40	1	100
Left atrial tumor					1	100
Transposition of great vessels	2	50				
Aortic-pulmonary window	1	100				
Tricuspid and pulmonary stenosis			2	0		
Aneurysm sinus of valsalva					1	100

tive risk for typical and straightforward cases and the reason for our confidence in the effectiveness of cardiopulmonary bypass can be gained only by more detailed study as given below. In general it might be stated that in our early experience, for example, the first 100 cases, only the more seriously ill patients were operated upon, some of whom would be declared inoperable at present. As confidence was gained, better risk patients were operated upon but without exclusion of those who were desperately ill and in need of correction. The latter fact is particularly evident in treatment of the tetralogy of Fallot, as in the last 18 cases all but one had been operated upon previously, many twice, and one three times with systemic-pulmonary anastomoses. All but 2 of the 18 patients were adults. A discussion is presented below of the individual lesions, the indications for operation, and fundamentals of treatment.

Aortic stenosis. Congenital aortic stenosis is discussed more fully in an accompanying article.[8] The results have been gratifying, 29 of 31 patients with an uncomplicated valvular or subvalvular stenosis surviving operation with a decrease in the aortic gradient and improvement in the clinical picture.

Aortic stenosis in the adult, we believe, has usually but not always been due to a congenital lesion in the patients we have treated, as evidenced by the absence of involvement of other valves and the similarity of the pattern of commissural fusion in adults and children. Regardless of the etiology, the end result is frequently a badly damaged valve resembling nothing as much as a bed of coral. Results in our recent experience improved when we abandoned the attempt to remove the calcium extensively and concentrated on mobilizing one or one and a half leaflets. Little can be accomplished with these valves unless adequate time is available for meticulous work upon the leaflets. In order to do this we have used perfusion of both coronary arteries and have witnessed on a number of occasions improvement in cardiac action and a decrease in electrocardiographic evidence of ischemia when first the left, and then the right, coronary artery was perfused. In some of the earlier cases in which coronary perfusion was not adequate there was evidence of myocardial infarction which we attributed to ischemia during the period of open cardiotomy. For these reasons we strongly prefer to perfuse both coronary arteries and not just the left coronary. Our most satisfactory method of perfusion to date has been with small balloon tipped catheters placed directly in the coronary orifices and held in with a purse-string suture. Perfusion is directly from the arterial line through the individual catheters. Perfusion in this manner is also used in children when a subvalvular stenosis is present. If a valvular stenosis is seen which can be readily cut, ischemic arrest for the necessary 5 to 10 min. may be used.

Removal of calcium from aortic leaflets, particular emphasis being upon the noncoronary leaflet, may in some cases result in a thinned-out and perforated valve. In such instances we have been encouraged with replacement of the cusp with a molded Teflon fabric prosthesis. This has been associated with virtual disappearance of the pressure gradient and diminution of preexisting aortic insufficiency in three patients.

Ventricular septal defect. This continues to be one of the more common lesions, one which can be treated with gratifying results. In patients under 25 pounds in weight, those with transposition of the great vessels, and a single patient with severe pulmonary hypertension and peripheral cyanosis (misdiagnosed as a single atrium) are excluded, only one death has occurred in the last 34 patients. This patient died with atelectasis in the early postoperative period.

We have temporarily stopped attempting to close the ventricular defect in infants in failure as the risk is prohibitive at the present time. Some infants with this condition have been treated by banding of the pulmonary artery with the anticipation of latter correction. One patient has been so treated with later closure of the ventricular defect and survival.

In older children we have urged closure of the ventricular defect if pulmonary hypertension is present because of the likelihood that the hypertension will progress and ultimately become irreparable. We believe it is significant that few adults with ventricular septal defect have been seen; the mortality is extremely high in these patients, probably because of irreversible pulmonary vascular changes. Operation has been advised for children with ventricular defect but without pulmonary hypertension if the pulmonary blood flow is extraordinarily high or if significant cardiac enlargement or other signs of failure are present.

In selecting patients with pulmonary hyper-

tension and ventricular septal defect for operation it is encouraging to have evidence of enlargement of the left atrium and left ventricle by roentgenography and electrocardiography and an increased pulmonary blood flow on cardiac catheterization. When the clinical evidence suggests that the work of the two ventricles and the resistance of the two circuits is approaching equality the risk of correction becomes prohibitive.

Tetralogy of Fallot. Because of the low risk and the great likelihood of considerable improvement after a subclavian-pulmonary anastomosis in young patients in contrast to a high mortality with bypass procedures, we continue to use the anastomotic procedure up to the age of about 6. Correction of a typical tetralogy in a child can be accomplished with considerably less risk than may seem indicated from the tabulated results. The high fatality rate is related to the age of the patients treated, an age that has often been attained only because of previous anastomotic shunts. All but one of the last 18 patients in this group had been operated upon previously, one having had three previous anastomotic procedures. Five of the last seven deaths resulted from massive bleeding and resulting complications in older children or adult patients. Only one of the deaths was in a child, and this patient had had two previous anastomotic operations, one of which was an end-to-end anastomosis. The ideal time for operation seems to be between 5 and 15 years of age; the small size of the heart in younger patients makes repair more difficult and hemorrhage associated with long-standing polycythemia is more frequent in older patients.

It has usually not been difficult to close a previous shunt if one approaches and mobilizes the subclavian artery from adjacent to the aortic arch. In many instances we have used this subclavian artery for cannulation and arterial return. A median sternotomy has considerably reduced the surgical hazard since neither chest has to be entered, and the collateral channels and the vascular adhesions need not be divided.

It is imperative that both infundibular and pulmonary valvular obstruction be relieved. Wide excision of the infundibular muscle and scar can usually be done and an adequate opening obtained. In some instances the pulmonary valve and adjacent pulmonary artery are small, and a patch must be inserted for enlargement. A portion of Teflon aortic prosthesis has worked most satisfactorily.

Atrial septal defect. The typical septum secundum atrial defect has been treated satisfactorily in our experience with hypothermia, caval occlusion and coronary perfusion, as described in a previous report.[6] In children this is a simple and highly effective method. We reserve cardiopulmonary bypass for adults and for the occasional patient in whom the diagnosis is not clear.

Ostium primum defects require the use of cardiopulmonary bypass in order that the mitral valve may be carefully inspected and sutured if necessary. In repairing this valve one must be certain that all available valve tissue is approximated. We have been guided in this by the attachment of chordae tendineae to the valve edge as sutures are placed from the top of the ventricular septum toward the free edge of the valve. A patch, usually Teflon felt, has been used in repair of the septal defect, care being taken to avoid the conduction tissue between the coronary sinus and the top of the ventricular septum.

Although minor anomalies of the pulmonary venous return can be readily treated with hypothermia and caval occlusion, total anomalous return and the more complicated or incompletely diagnosed lesions can best be treated with the additional time allowed by cardiopulmonary bypass. Our earlier experiences with this have been reported.[1]

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REFERENCES

1. Bahnson, H. T., Spencer, F. C., and Neill, C. A.: Surgical treatment of thirty-five cases of drainage of pulmonary veins to the right side of the heart. J. Thoracic Surg., *36:* 777, 1958.
2. Boyd, A. D., Tremblay, R. E., Spencer, F. C., and Bahnson, H. T.: Estimation of cardiac output soon after intracardiac surgery with cardiopulmonary bypass. Ann. Surg., *150:* 613, 1959.
3. Helmsworth, J. A., Kaplan, S., Clark, L. C., Jr., McAdams, A. J., Matthews, E. C., and Edwards, F. K.: Myocardial injury associated with asystole induced with potassium citrate. Ann. Surg., *149:* 200, 1959.
4. Kay, J. H., and Gaertner, R. A.: A simplified pump oxygenator with flow equal to normal

cardiac output. Surgical Forum, 42nd Clinical Congress American College of Surgeons, *7:* 267, 1956.

5. SPENCER, F. C., AND BAHNSON, H. T.: The use of ethylene oxide for gas sterilization of a pump oxygenator. Bull. Johns Hopkins Hosp., *102:* 241, 1958.
6. SPENCER, F. C., AND BAHNSON, H. T.: Intracardiac surgery employing hypothermia and coronary perfusion performed on 100 patients. Surgery, *46:* 987, 1959.
7. SPENCER, F. C., BENSON, D. W., AND BAHNSON, H. T.: Use of a mechanical respirator in the management of respiratory insufficiency following trauma or operation for cardiac or pulmonary disease. J. Thoracic Surg., *38:* 757, 1959.
8. SPENCER, F. C., NEILL, C. A., SANK, L. AND BAHNSON, H. T.: Anatomical variations in 46 patients with congenital aortic stenosis. Am. Surgeon, *26:* 204, 1960.
9. STURTZ, G. S., KIRKLIN, J. W., BURKE, E. C., AND POWER, M. H.: Water metabolism after cardiac operations involving a Gibbon-type pump-oxygenator. Circulation, *16:* 988, 1957.
10. THISTLETHWAITE, J. R., SPENCER, W. A., AND ALBERT, S. N.: Blood volume fluctuations determined by radioisotopes of chromium and radioactive iodinated serum albumin. Surg. Gynec. & Obst., *105:* 34, 1957.
11. WILLIAMS, G. R., JR., AND SPENCER, F. C.: The clinical use of hypothermia following cardiac arrest. Ann. Surg., *148:* 462, 1958.

SIX CASE HISTORIES DEMONSTRATING THE FEASIBILITY OF PARTIAL OR TOTAL REPLACEMENT OF VERTEBRAL BODIES BY BONE GRAFTS

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During recent years several papers have been published demonstrating increased interest in surgery of the vertebral column. Studies and experimentation have led to the adoption of known surgical exposures of the spine to new uses. In addition to the interest in approaches to the cervical, thoracic and lumbar spine for open biopsy and drainage[5] more attention has been devoted in the last 10 years to the possibility of doing something definitive about existing pathology after its exposure particularly when it is due to trauma, infection or a benign tumor.

Bone grafting of vertebrae is not new, but with increased interest in exposure and surgical treatment of the spine several new techniques of fusing vertebrae have been developed.[2, 6-9] Most of the published reports have dealt with the grafting of autogenous or homogenous bone across the area of osseous pathology—posteriorly, anteriorly or laterally. Only very few[4] of the papers which have come to our attention have specifically mentioned total or almost total replacement of vertebral bodies by a bone graft, although Erlacher[2] and Hodgson[3] and others[1] have replaced vertebral bodies destroyed by infection and tumor with such a graft.

The purpose of this paper is to report our experience in 6 patients in whom because of tumor, trauma or infection a vertebral body was destroyed to the point where it was useless as a weight bearing structure and had to be replaced by autogenous or homogenous bone.

Five of the cases are from the Orthopedic Service of The Johns Hopkins Hospital and the Baltimore Children's Hospital. The sixth case is contributed by Doctors Lipinski and Taxdal of Lakeland, Florida. Together these cases demonstrate several of the known methods of partial and total replacement of destroyed vertebral bodies. These were performed by different operators and demonstrate the forms of grafts used: (1) struts wedged into normal vertebral bodies above and below the pathology with and without associated posterior fusions, (2) Solid intervertebral blocks and (3) multiple chips or bone meal in addition to intervertebral body struts. All bone grafts were put directly into the spinal defect after excision of the diseased or traumatized bone rather than lying over the top of and bridging the diseased area. The diseased bone was replaced with nondiseased bone as a graft which structurally stabilized the spine, within the limits of the graft strength, until fusion occurred.

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CASE REPORTS

Case 1. D. L. (B-54096), a 3½-year-old white boy was transferred to The Johns Hopkins Hospital from Hagerstown, Maryland, on August 6, 1958, with a diagnosis of tuberculosis of the 3rd lumbar vertebral body after 2 months' treatment with para-aminosalicylic acid (PAS) and isonicotinic acid hydrazide (INH) and bed rest. History of exposure to tuberculosis was negative, but the 2nd strength purified protein derivative of tuberculin (PPD) was positive. His mother had first noticed that he walked with his lumbar spine straight and that he complained of mild pain in the midline of his back while upright.

X-rays upon admission revealed a destructive lesion of the body of L-3 and a left chest infiltration. There were no positive physical findings other than slight prominence of L-3–4 spinous processes coincident with a loss of lumbar lordosis.

Biopsy and curettage of the lower part of L-2, all of L-3 and the upper part of L-4 was done on August 15, 1958, through a left transverse abdominal sympathectomy incision. The involved vertebrae were approached retroperitoneally. Soft cystic and fibrous tissue was removed from this area and homogenous rib graft was inserted into the gap thus created between the upper half of the body of L-2 and the body of L-4, utilizing additional bone chips to supplement the rib graft.

Postoperatively, bed rest in a full length plaster

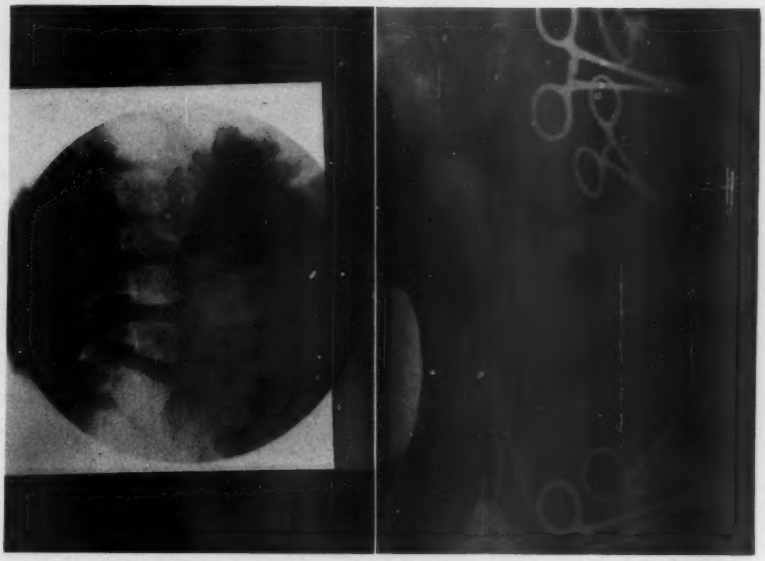

FIG. 1. *Case 1.* A 3½-year-old boy was admitted on August 6, 1958, to The Johns Hopkins Hospital with diagnosis of tuberculosis of L-3 vertebra. Symptoms were of mild pain in his back. Lumbar spine was held straight and stiff while walking.

Note collapse of anterior portion of L-3 with narrowing of L-2–L-3 interspace and L-3–L-4 interspace. Posterior elements not involved. Picture on *right* is marker film taken in operating room after the body of L-3 had been for all practical purposes removed and only about ¾ of the periphery of the L-2–3 and L-4–5 intervertebral discs and the superior half of the body of L-2 remained after the abnormal tissue had been removed.

cast from shoulders to toes was used for 3 months, and thereafter, the child was ambulated in a ½-leg hip-body spica for 3 months, followed by a body cylinder for 3 months with both legs free. Cultures were negative for tuberculosis. No paravertebral abscess was present. Pathology report was chronic inflammatory disease without giant cells or tubercles, but the possibility of a healed tuberculosis or nontuberculous osteomyelitis, or even an unusual form of Hand-Schüller-Christian disease was thought possible on the basis of the microscopic pathology. Immobilization was discontinued 16 months postoperatively when the interbody fusion appeared to be completely consolidated. Antituberculous medication was discontinued after 18 months.

Case 2. H. S. (802655), a 56-year-old white man arrived at The Johns Hopkins Hospital Accident Room on March 28, 1959, holding his head with his hands after having suffered a "sprain" type injury. The patient's complaints of transient weakness and paresthesias in his neck and upper extremities followed his involvement in an automobile collision in which his car was struck from behind.

X-ray revealed a pathologic fracture through the body and dens of C-2. Skull tongs were inserted immediately, and 20 lb. of traction were applied. The patient remained thus on bed rest until posterior stabilization of the occiput to C-4 had been obtained; his own iliac bone was used for grafting material by Dr. Wayne Southwick. This fusion procedure was reinforced with no. 20 stainless steel wire.

The diagnosis of gout in relation to previous episodes of pain in the great toe and an abnormally elevated serum uric acid determination suggested the possibility of a tophaceous lesion of the body of C-2. Posterior cervical spine fusion was successful, and the patient was discharged in a Minerva jacket. Three months later a four-poster neck brace was used for an added three months.

Subsequent spells of dizziness a year later and review of spinal x-rays revealed fusion of the posterior graft with neck stability but progressive destruction of C-2. Clinical control of gout by Benemid had been maintained throughout the intervening year. On April 27, 1959, he underwent biopsy of C-2, a debridement at the C-2 body region of a soft reddish colored tumor, and fusion

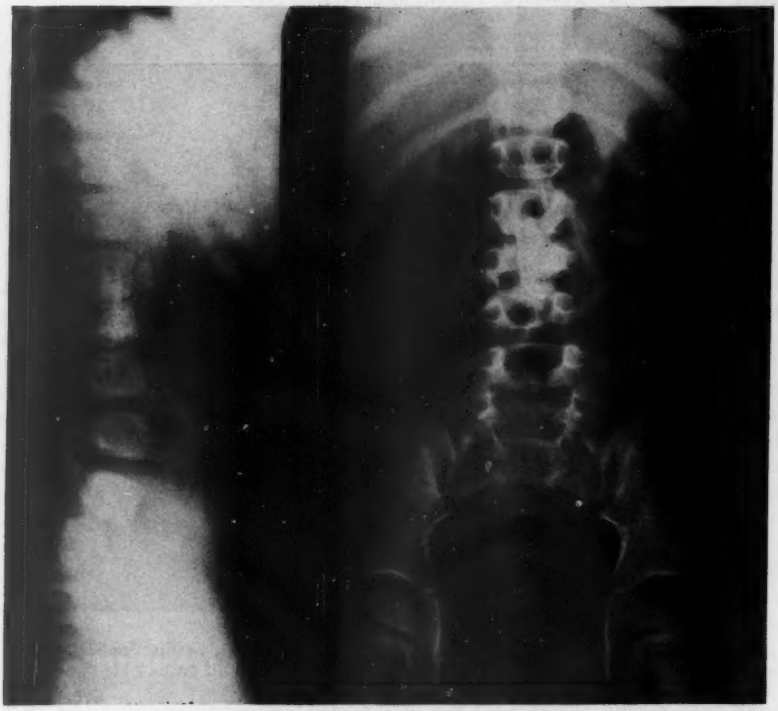

FIG. 2. *Case 1.* Nine-month postoperative film revealing rib graft and bone chip placement in the diseased area of L-2 and L-3. Pathologic report was not conclusive for tuberculosis and was described as being compatible with chronic inflammatory changes of an aborted osteomyelitis or possibly of a Hand-Schüller-Christian disease. Patient ambulatory without cast 16 months postsurgery and asymptomatic.

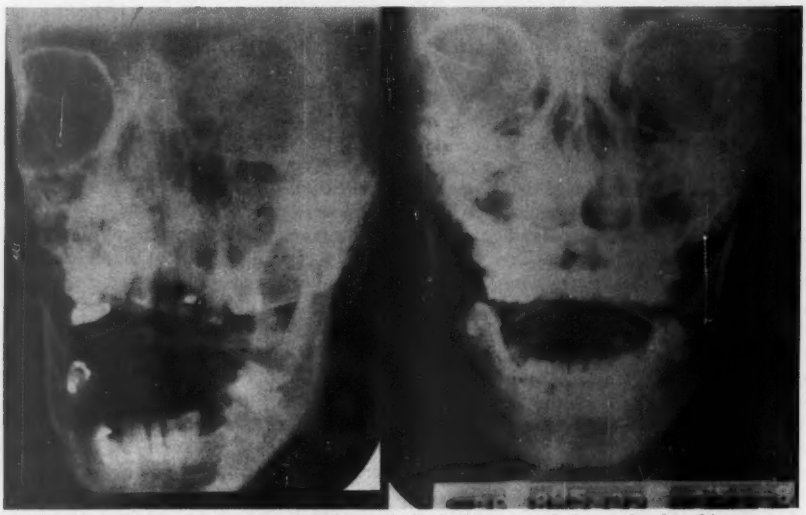

FIG. 3. *Case 2.* A 56-year-old man suffered a pathologic fracture of the neck when his car was struck from behind on March 27, 1958. He walked into The Johns Hopkins Hospital Accident Room with subjective complaints of transient paresthesias in his hands and neck. Note fracture of C-2 and base of odontoid through what appears to be pathologic bone of C-2. Patient put in skull tongs and 20 pounds of traction resulting in immediate subsidence of paresthesias.

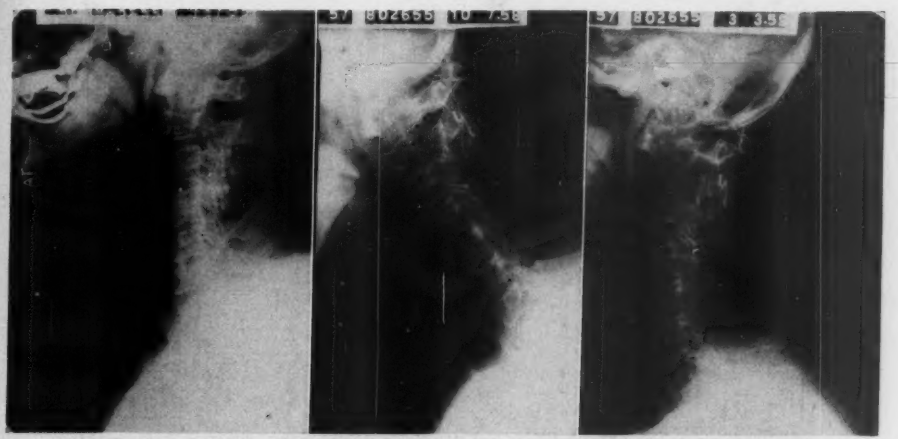

FIG. 4. *Case 2.* Film on *left* was taken in traction the night of admission. Note sharp edges of vertebral body accentuating destroyed area in center of body. Fusion was done posteriorly from occiput to C-4 utilizing autogenous iliac graft 3 weeks after admission. Patient was put in Minerva jacket 4 weeks postoperatively. The *center* film was made when the neck was stable 6 months after posterior bone graft. The film on the *right* shows the neck about 1 year after posterior neck fusion. The body of C-2 and some of the facet region of C-2 had continued to disappear since the posterior fusion. The bone replacement was subsequently found to be due to a monostotic plasma cell myeloma.

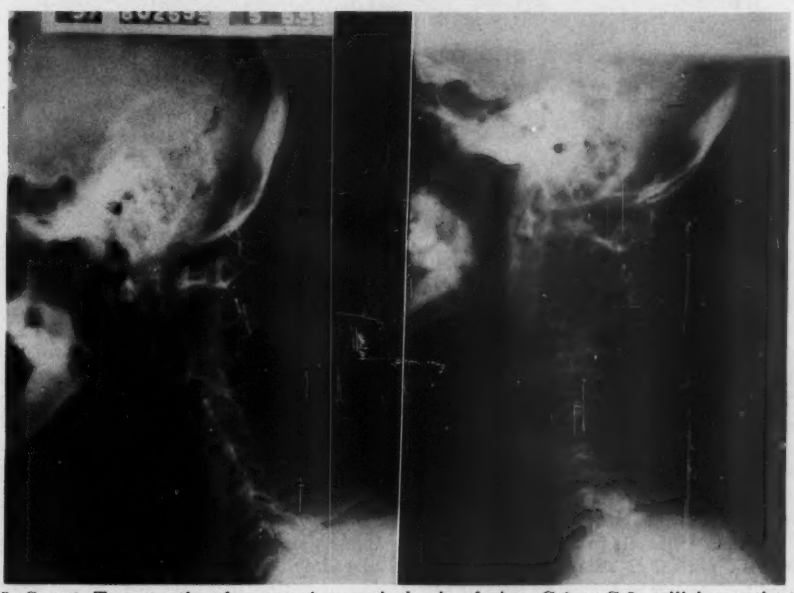

FIG. 5. *Case 2.* Two months after anterior cervical spine fusion, C-1 to C-3, utilizing patient's own tibial bone as a graft, and one month after x-radiation of region of body of C-2 for monostotic plasma cell myeloma. Extension and flexion films are shown to demonstrate rigidity of neck due at this time to posterior fusion.

of C-1, C-2 and C-3 from the anterior approach.[8] This fusion utilized a tibial bone graft from the patient. The pathology diagnosis was plasma cell myeloma. Skeletal survey and bone marrow biopsy were negative at the time for similar lesions in other bones. One month later 3500 roentgens skin dose over the body of C-2 was given over a 3-week period. The patient appeared well and active in

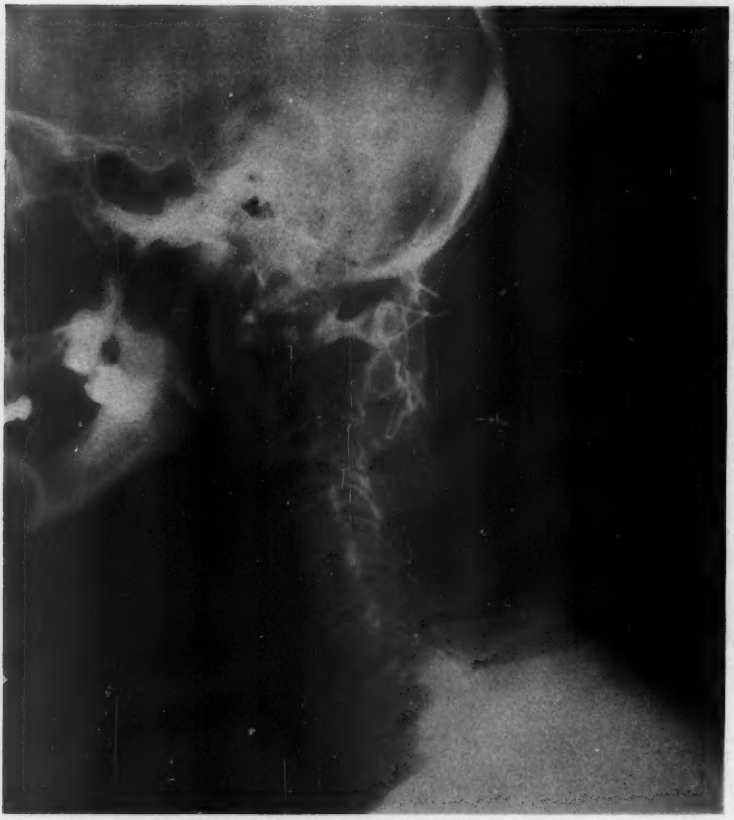

FIG. 6. *Case 2.* Fifteen months after fusion of posterior elements of occiput to C-4 and four months after fusion of anterior ring of C-1 to body of C-3. Graft appears solidly fused to body of C-3 but not yet definitely fused to anterior ring of C-1.

his profession 4 months after anterior fusion and x-ray therapy.

Case 3. T. T. (12976), a 3-year-old colored girl was admitted to Children's Hospital on August 5, 1959, with a diagnosis of tuberculosis of L-1. There was a strong positive family history of tuberculosis with adequate history of recent contact. A patch test was positive. Her mother noticed that after a fall from a tricycle in May 1959 the child did not walk normally. This gait abnormality progressed to inability or refusal to walk.

Positive findings on admission to the Children's Hospital were psoas spasm, gibbus in the L-1 area and hyperreflexia of the lower extremities. INH, 50 mg. twice a day, and PAS, 1 gm. 3 times daily were started after x-rays revealed a destructive lesion of L-1 and L-2. A full length body cast from shoulders to toes was made before surgery and then bivalved for postoperative use as turning shells.

Through a left sympathectomy approach[9] on September 12, 1959, resection of the left 12th rib, curettage of the lower half of the body of T-12, all of the body of L-1 and the upper half of the body of L-2 were carried out. The gibbus was corrected and matchstick grafts of homogenous tibial cortical bone were inserted and the rest of the defect was filled with ground bone. Postoperatively the cast was reapplied, and the patient was placed on bed rest and continued on drugs as before operation. The pathology report was "granulation tissue reaction with multinucleated giant cells compatible with tuberculosis."

Case 4. B. L. (596308), a 15-year-old white girl was admitted to the neurosurgical service of The Lakeland Hospital, Lakeland, Florida, with a single bullet wound of the neck. There was x-ray evidence of destruction of the body of the C-4 vertebra and physical signs of a Brown-Sequard syndrome below C-4, a left upper extremity mono-

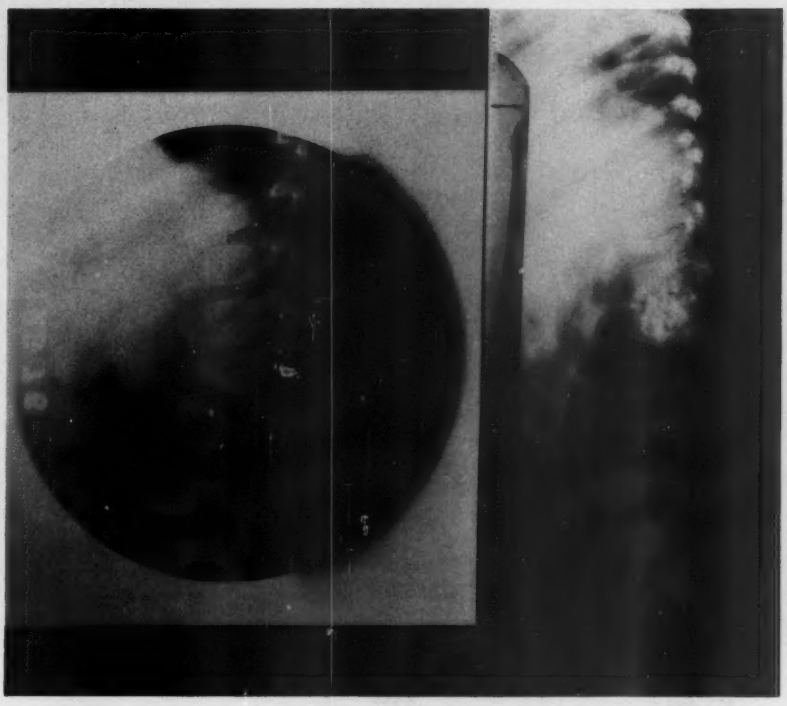

FIG. 7. *Case 3.* A 3-year-old colored girl was admitted to Children's Hospital with history of a recent fall from tricycle and inability to walk well thereafter. Strong family history of tuberculosis. Gibbus on physical examination at L-1. Hyperactive deep tendon reflexes in lower extremities. Note total destruction of L-1 body with partial involvement of the T-12 and L-2 bodies as well. Film on *right* is postoperative 1 week. Complete removal of L-1 body, the lower half of the T-12 body, the upper portion of the body of L-2 and the T-12–L-1 and L-1–L-2 discs was carried out. Grafts consisted of cortical struts and ground bank bone. Appearance of ground bone fragments posterior to the vertebral bodies in the midline is an illusion; that bone is actually lateral to the spinal canal, lying in the interval between the transverse processes.

plegia, and a monoparesis of the left lower extremity.

Subsequently, after institution of skull traction the cervical spine was approached through a "collar" incision[9] and the body of C-4 appeared to be completely exploded. All loose bone fragments were removed. Disc material at C-3–C-4 and C-4–C-5 had been disorganized, and so the fragments of these two discs were also removed. An iliac bone graft was cut to fit the defect thus created and placed therein. Seven days postoperatively in a cervical brace, the patient was ambulated and soon returned to high school. The level of sensory loss on the right side began to recede postoperatively, and use was gradually regained in the left upper extremity. External cervical support is planned for 3 months.

Case 5. C. N. (802058), a 14-year-old white girl was admitted to The Johns Hopkins Hospital in April 1958 for the removal of a painful mass in the left popliteal space. She had been followed in the Harriet Lane Home Out-Patient Department for several years because of mental deficiency, psychomotor seizures and left hemiparesis. At surgery, a smooth, well encapsulated tumor was easily removed from the left popliteal space. She was discharged and returned to school free of symptoms. Pathologic report, however, was neurofibrosarcoma, rather than von Recklinghausen's neurofibromatosis, as first diagnosed.

Her next admission was January 11, 1959, because of pain of one week's duration in her neck. Clinically, there was acute pain upon any attempted motion of her neck. Extreme tenderness over a mass on the back of her neck was present at C-5 and C-6. X-rays revealed a bone displacing lesion in the anterior portion of C-5 and the spinous processes of C-5 and C-6. Neurologic examination was unchanged from that recorded previously.

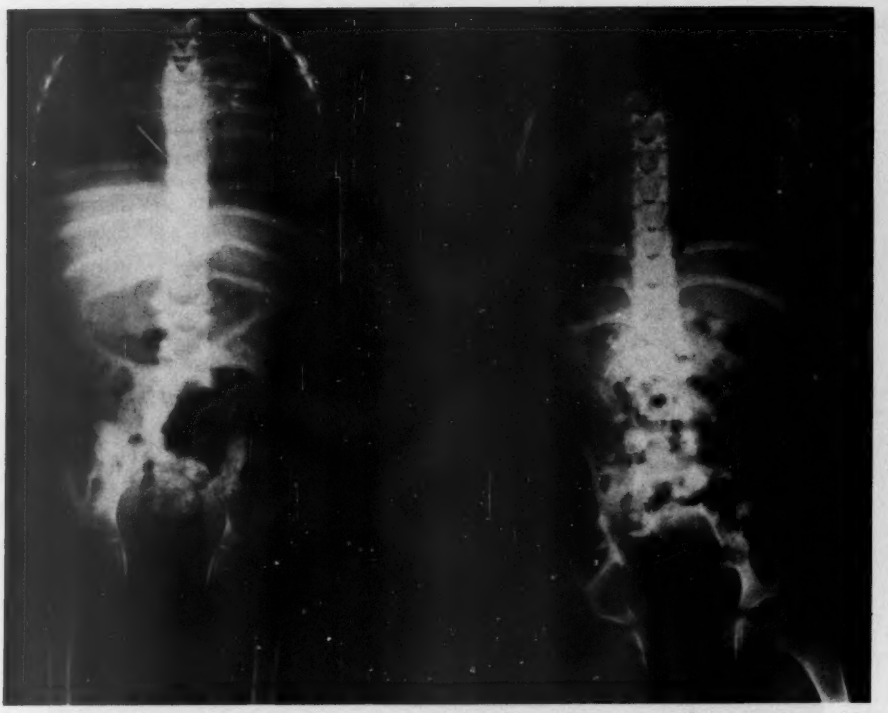

FIG. 8. *Case 3.* Pre- and postoperative anteroposterior views of the spine. The appearance of bone lateral to the interbody fusion site is occasioned by bone placed laterally between the transverse processes of T-12, L-1 and L-2.

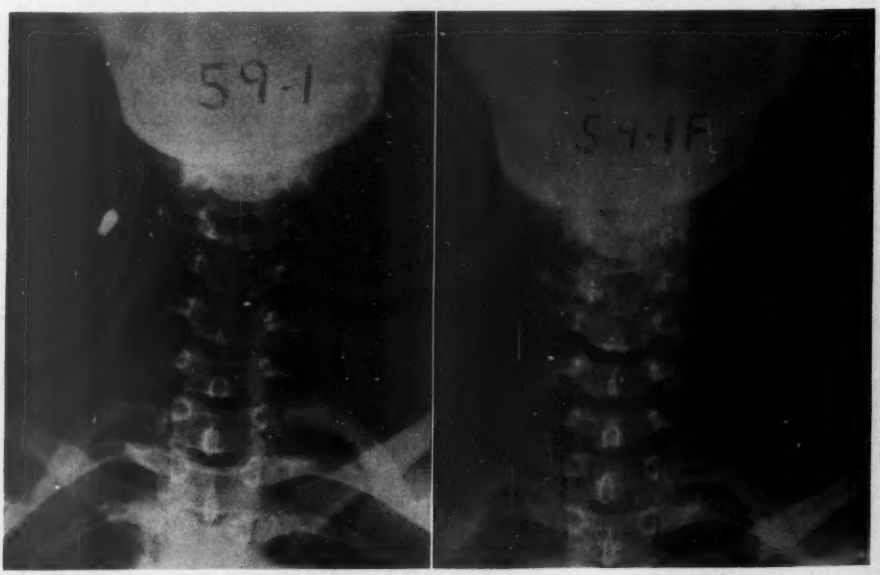

FIG. 9. *Case 4.* A 15-year-old white girl with bullet wound to C-4 resulting in Brown-Sequard syndrome plus left upper monoplegia and left lower monoparesis. Note that the left facet joint of C-4 has been shattered by missile after its course completely through the body of C-4. Lumbar puncture was normal. Posterior decompression was not done. The x-ray on the *right* was made postoperatively.

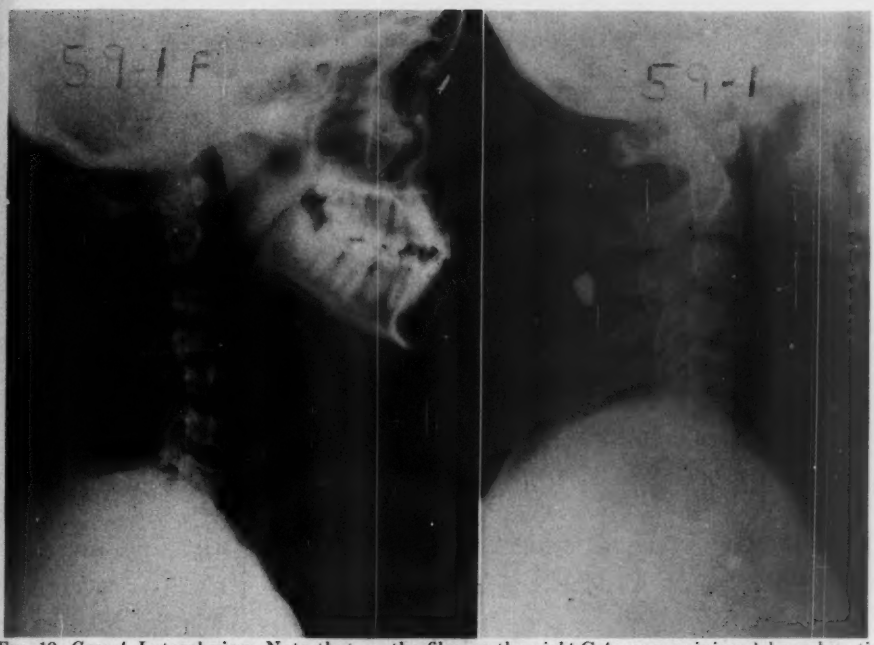

FIG. 10. *Case 4.* Lateral view. Note that on the film on the *right* C-4 appears injured by a bursting fracture that causes slight posterior displacement of the back of the vertebral body and anterior displacement of the front of the vertebral body. However, the extent of injury that was evident at surgery is not obvious on these films. Disc material at C-3–C-4 and C-4–C-5 was also disorganized. The film on the *left* is the postoperative film. Note shadow of the iliac graft between C-3 and C-5. This patient ambulated at 7 days in a 4-poster brace and has shown steady improvement neurologically.

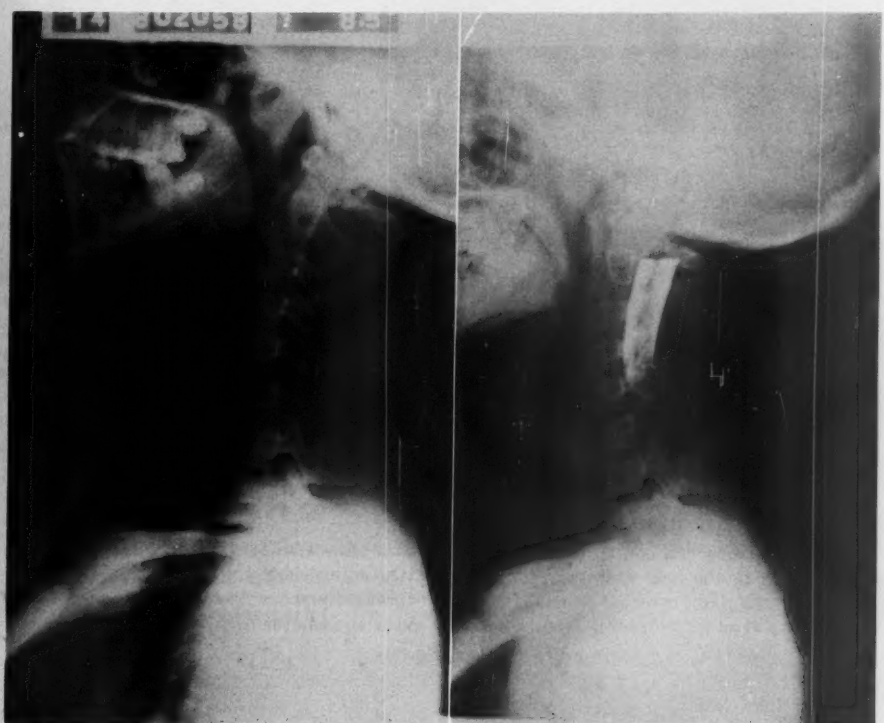

FIG. 11. *Case 5.* Preoperation x-ray and myelogram showing destruction of the posterior elements of the 6th cervical vertebra including the facet joints.

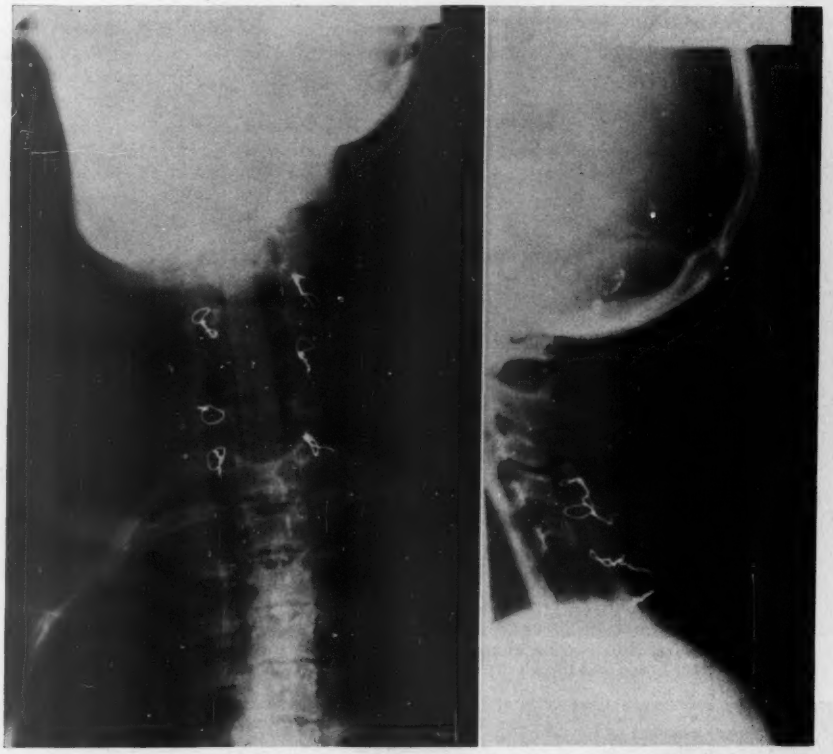

FIG. 12. *Case 5.* Postoperative x-rays showing the posterior bilateral iliac bone struts attached to the facet joints by wire loops at the time of the laminectomy and the anterior tibial bone strut running from C-3 to T-1 placed anteriorly at the second operation when the body of C-6, which was almost entirely replaced by neurofibrosarcoma, was excised.

The left popliteal space was enlarged and tender again.

Crutchfield tongs were inserted and the child was placed on a Stryker frame. A cervical myelogram performed January 13, 1959, demonstrated a complete block from C-5 to T-1. January 16, 1959, a posterior laminectomy was carried out at C-4–C-7. The tumor was found to be widely infiltrating and encompassed the extradural space from C-4 to C-7. The dura was not involved other than by pressure. Posterior fusion was done at the time of laminectomy with the use of iliac grafts wired bilaterally to the facet joints of C-3 to T-1 inclusive. Postoperatively, she demonstrated impairment of sensation below T-1 and marked motor weakness below C-5 bilaterally. This gradually improved in the immediate postoperative period so that she could move all extremities.

On February 24 an anterior cervical spine fusion was performed by utilizing a vertical incision along the anterior border of the sternocleidomastoid muscle.[8] A long strut of her own tibial bone was inserted into a trough created in the bodies of C-4, C-5, C-6 and C-7. Its ends were inserted into the inferior part of the body of C-3 and the superior part of the body of T-1, thus bridging the gap of destroyed bone at C-5 anteriorly. The tumor was removed from the region of the body of C-5, but more tumor was then seen extending into the spinal canal through the posterior longitudinal ligament at this level.

On March 4, 1959, she was discharged in a Minerva jacket with motion present in all four extremities (pre-existing left hemiparesis) but with diminished strength. Pathologic diagnosis of neurofibrosarcoma was returned on the tumor specimen from the neck. A total of 1600 roentgens

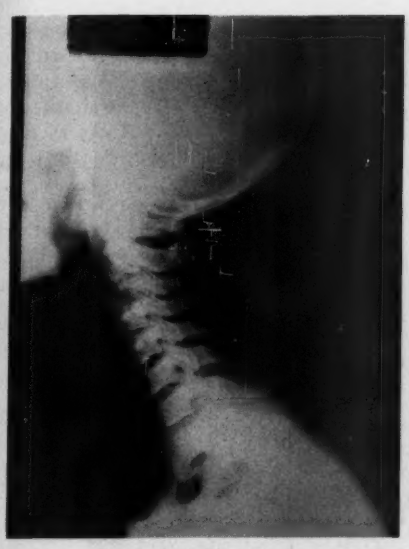

FIG. 13. *Case 6.* This film of F. S., 14-year-old white boy, taken on admission to hospital demonstrates clearly the collapse and radiolucency of the 3rd cervical vertebral body.

was given through 3 skin portals despite impression that tumor would be insensitive to x-ray.

She was seen as an out-patient 3 times in April and demonstrated a progressive downhill course from her disease, but revealed x-ray evidence of fusion of the posterior and anterior grafts with resultant removal of the cast for comfort. She expired in May 1959, 3 months after the last operation.

Case 6. F. S. (849995), a 14-year-old white boy was admitted to The Johns Hopkins Hospital medical service on June 13, 1959, because of complaints of pain in the neck.

The only past history of any possible significance was that of a bout of pneumonia treated successfully with 2 million units of penicillin during the summer of 1958.

Three weeks prior to admission, he had experienced sudden onset of pain and stiffness in his neck when he was moving bricks in a wheel barrow. Pain was increased 1 week before admission when he slid back suddenly in a reclining chair; this pain was followed by numbness and tingling of his fingers.

X-rays revealed a destructive lesion of the body of C-3. Neurologic examination was negative, but

FIG. 14. *Case 6.* Picture on *left* taken as a localizing film at time of surgery. Point of needle is seen in the area of the destructive lesion of C-3. On the *right*, one can see the cortical strut in place after surgery, but before the tongs and cervical traction were removed Note the cancellous portion of tibial graft anterior to its cortical portion.

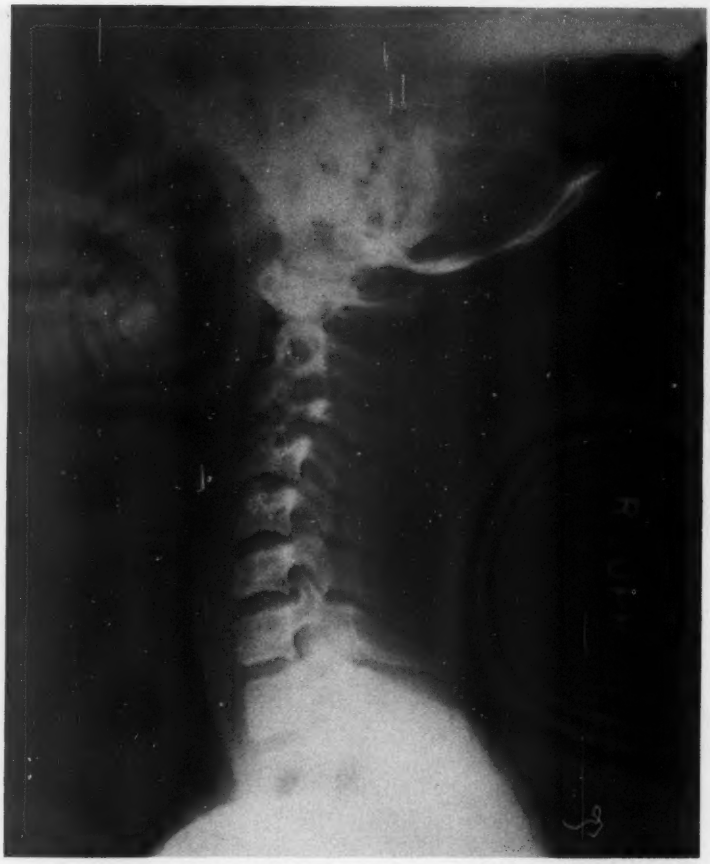

FIG. 15. *Case 6.* Four-month postoperative film illustrating apparent fusion of C-2–C-4 with generous new bone formation. Outline of cortical portion of graft still visible.

he couldn't sit up or tolerate head motion on admission. The only positive laboratory finding was a phosphorus of 7.4 mg. per cent and an alkaline phosphatase of 20.6 Bodansky Units—both elevated. Through a vertical anterior approach biopsy was performed and partial removal of the soft tissue replacing the 3rd cervical body, and fusion of C-2 to C-4 was performed utilizing a graft from the patient's tibia. The abnormal tissue was not very vascular but pulsated, apparently because the vertebral arteries ran through it. *Escherichia coli* was cultured from this tissue, and on histologic examination the material was compatible with a diagnosis of chronic osteomyelitis of C-3. Two weeks postoperatively the patient was removed from traction and a Minerva jacket was applied. Postoperatively the patient had no difficulty and at present, 5 months postsurgery, the patient is ambulating comfortably without evidence of neurologic deficit, and the region between the bodies of C-2 and C-4 is filling in with bone.

SUMMARY

Six cases have been reported, with photographs of relevant roentgenograms demonstrating destruction or extensive damage of cervical and lumbar vertebrae by infection, tumor or trauma.

These cases all illustrate the feasibility of direct surgical attack upon the diseased area with replacement of the diseased vertebral bodies by

bone grafts. Collapse of the vertebral column was thus prevented, and more rapid and safe mobilization of the patients was achieved. Demonstrated, too, is the advantage of direct biopsy to give accurate diagnosis in destructive lesions of the vertebral bodies.[5]

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REFERENCES

1. Bailey, R. W., and Badgley, C. E.: The role of anterior interbody cervical fusion in traumatic fracture dislocations and "spontaneous" dislocations following previous cervical laminectomy. J. Bone & Joint Surg., *41-A:* 768, 1959.
2. Erlacher, P. J.: Surgery in spinal tuberculosis. J. Bone & Joint Surg., *38-A:* 923, 1956.
3. Hodgson, A. R., Hong Kong. Personal Communication.
4. Ito, H., Tsuchiya, J., and Asami, G.: A new radical operation for Potts disease. J. Bone & Joint Surg.; *16:* 499, 1934.
5. Johnson, R. W., Jr., Hillman, J. W., and Southwick, W. O.:The importance of direct surgical attack upon lesions of the vertebral bodies particularly in Pott's disease. J. Bone & Joint Surg., *35-A:* 17, 1953.
6. Osmond-Clarke, H.: Pain in the arm of cervical origin. J. Bone & Joint Surg., *37-B:* 515, 1955.
7. Robinson, R. A., and Smith, G. W.: Anterolateral cervical disk removal and interbody fusion for cervical disk syndrome. Bull. Johns Hopkins Hosp., *96:* 223, 1955.
8. Smith, G. W., and Robinson, R. A.: The treatment of certain cervical-spine disorders by anterior removal of the intervertebral disc and interbody fusion. J. Bone & Joint Surg., *40-A:* 607, 1958.
9. Southwick, W. O., and Robinson, R. A.: Surgical approaches to the vertebral bodies in the cervical and lumbar regions. J. Bone & Joint Surg., *39-A:* 631, 1957.

IATROGENIC INTRAPERITONEAL DISSEMINATION OF A FIBROSARCOMA OF THE ABDOMINAL WALL*

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The accidental transplantation of tumor cells to the operative wound during surgical procedures for malignant neoplasms has been recognized for many years. In the recent past, much attention has been devoted to the general problem of dissemination of tumor by the surgeon, particularly with reference to blood stream spread. Although in certain circumstances there can be little doubt as to the relationship between the surgeon's manipulation and the subsequent development of metastases, the cause and effect relationship is difficult or impossible to establish in the case of intraperitoneal neoplasms in which serosal implants are noted to develop subsequent to surgery. Although iatrogenic dissemination of tumor cells in this situation seems highly probable in many instances, the spontaneous development of peritoneal metastases occurs with sufficient frequency in the natural history of such neoplasms to preclude precise differentiation between these two mechanisms of spread.

In a patient seen recently at The Johns Hopkins Hospital, however, there can be no doubt as to the iatrogenic origin of the serosal implants. This case so clearly demonstrates the danger of intraperitoneal dissemination of tumor during surgical procedures that it is deemed worthy of note. A second aspect which merits consideration concerns the nature and behavior of lesions arising in the abdominal wall. Although such lesions have come to be lightly regarded by many individuals, such an attitude is unjustified and dangerous. The fallacy of this view is clearly demonstrated by the distressing sequelae which resulted in this patient. The tumor in this patient was histologically a fibrosarcoma, a further point of interest since recorded instances of accidental transplantation of connective tissue malignancies are quite rare.

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CASE REPORT

R. G., a 37-year-old Caucasian man, was first admitted to The Johns Hopkins Hospital in May 1957 because of severe abdominal pain.

The family history and past history were noncontributory.

During October 1956 a laparotomy had been performed at another hospital because of epigastric and left-sided abdominal pain, thought to be due to a peptic ulcer with pyloric obstruction. A posterior gastroenterostomy was performed. In the course of the operation, a mass "about the size of a small lemon" was noted in the left upper quadrant of the abdominal wall. An "incision was made over the tumor mass from the inside of the abdominal wall and it was excised." It appeared grossly to be well encapsulated. Microscopic examination revealed the tumor to be a cellular fibrosarcoma (fig. 1).

Within 3 months, several nodules had appeared in the abdominal wall in the region of the previous tumor. These became progressively more painful, and resulted in the patient's admittance to The Johns Hopkins Hospital late in May 1957. Physical examination at that time was unremarkable except for 3 firm, discrete, tender nodules within the left upper quadrant of the abdominal wall just lateral to a well healed left rectus scar. The hemogram was within normal limits, and an x-ray of the chest was unremarkable.

On June 5, 1957, resection of this local recurrence was performed. The scar of the previous surgical incision was excised, medial and lateral skin flaps were raised and the peritoneal cavity entered in the midline, well medial to the gross tumor. Directly beneath the externally palpable masses, tumor was found to have grown through the posterior rectus sheath and parietal peritoneum and into the omentum which was adherent to the scar of the old incision. The most striking observation, however, was the presence of tumor implants scattered diffusely over the serosal surfaces of the peritoneal cavity (fig. 2).

Although a curative procedure was obviously impossible, a palliative *en bloc* resection of the abdominal wall recurrence was carried out to relieve the severe pain which was the patient's

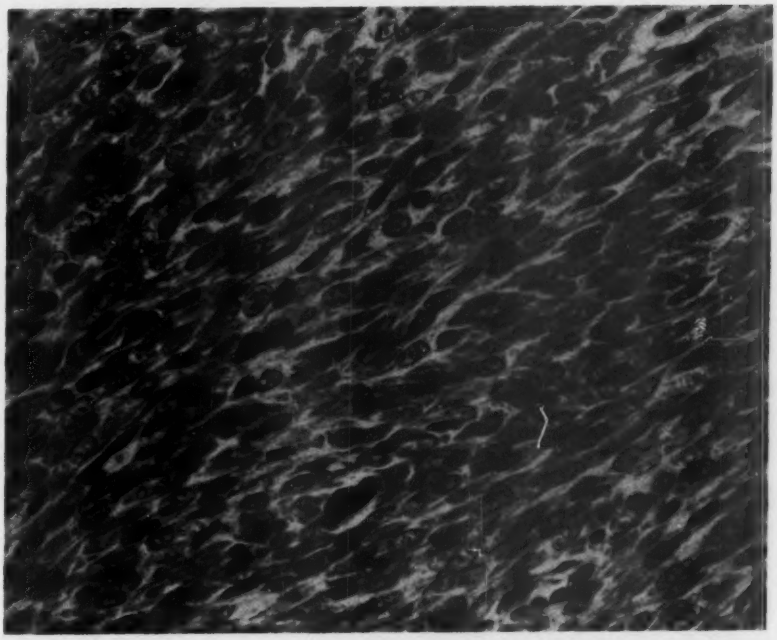

FIG. 1. Photomicrograph (× 500) of the tumor excised at the original operation in October 1956. Note the uniformity of the cells, virtual absence of fibrogenesis, and the lack of mitotic figures and abnormal mitoses.

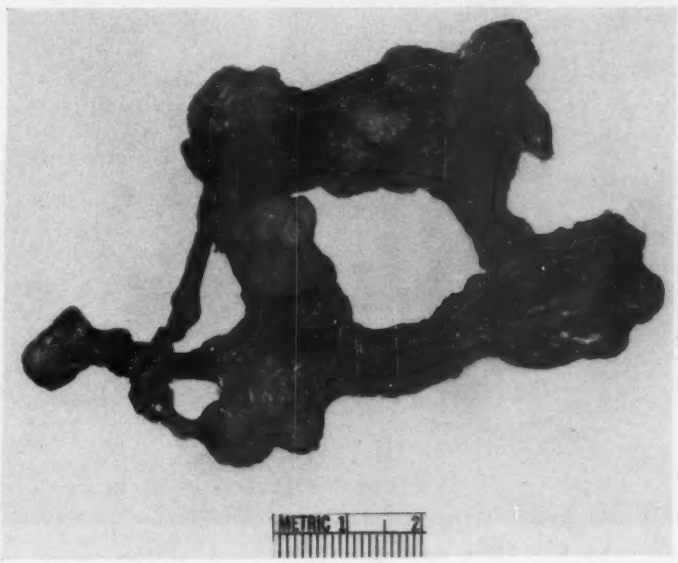

FIG. 2. Photograph of a portion of the omentum, distant from recurrent tumor in the abdominal wall, excised at the second operation in June 1957. Note the multiple tumor implants present in this small specimen.

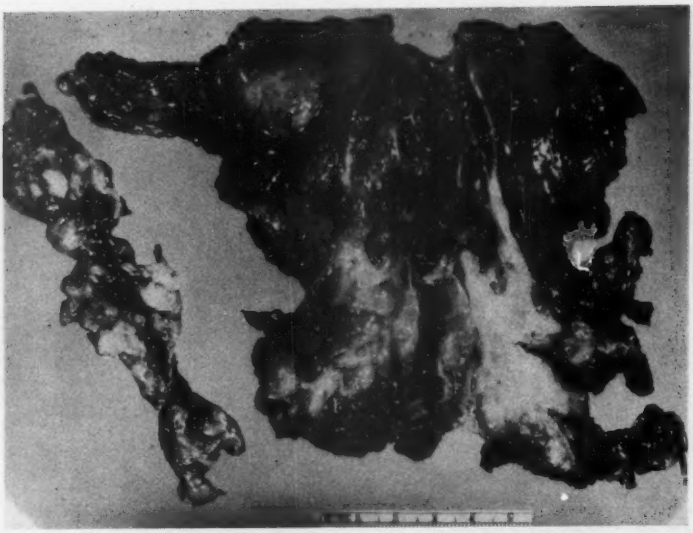

FIG. 3. Photograph of the serosal surface of the segment of the abdominal wall resected at the second operative procedure, showing invasion of tumor directly through the parietal peritoneum.

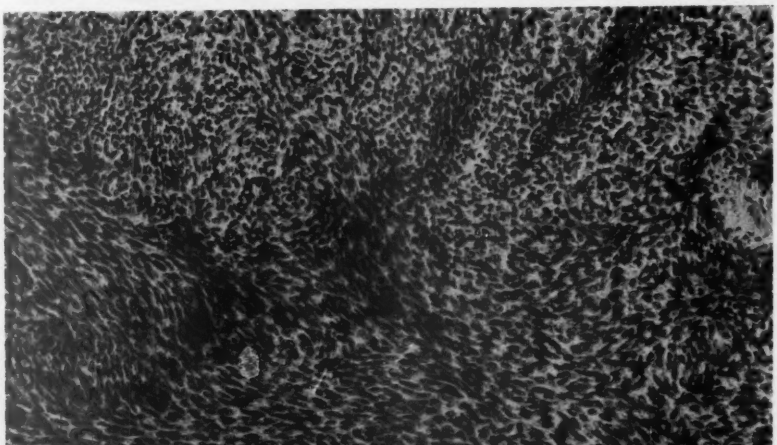

FIG. 4. Photomicrograph (× 150) of the recurrent tumor excised at the second operation. Note the extreme cellularity of the tumor.

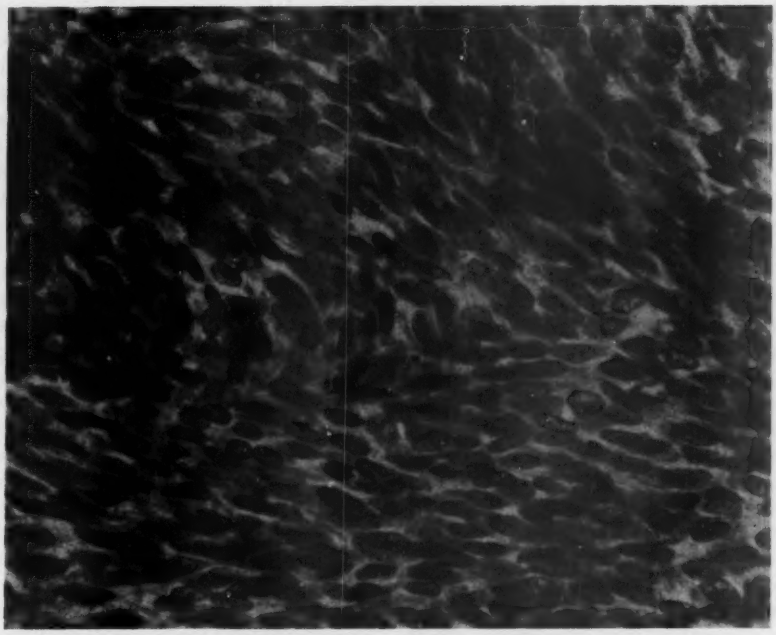

FIG. 5. Photomicrograph (× 500) of a peritoneal implant found at the second operation. The characteristics are identical to those of the original tumor and the abdominal wall recurrence.

only symptom. The resulting defect was closed utilizing tantalum mesh.

The specimen measured 15 by 18 cm. and included the full thickness of the abdominal wall (fig. 3). Within the specimen were several white nodules of tumor which for the most part were confined within the abdominal wall musculature but at one point extended directly through the parietal peritoneum. Microscopic examination (fig. 4) revealed the tumor to be a fibrosarcoma composed of densely packed, uniform cells which demonstrated minimal fibrogenesis and only rare mitotic figures. Histologic preparations of the diffuse implants revealed identical findings (fig. 5).

The patient's immediate postoperative course was unremarkable. In December 1957, 6 months after his second operation, he again complained of abdominal pain which was now associated with vomiting. Examination at that time revealed a 5 by 5 cm. mass in the midline just below the umbilicus and several smaller nodules beneath the tantalum mesh. Roentgenographic study of the upper gastrointestinal tract revealed extrinsic pressure defects of the stomach, gastroenterostomy and distal duodenum due to a large mass in the left upper quadrant. A chest film at that time was normal.

His subsequent course was one of rapidly increasing weakness and weight loss. He was treated with 5-fluorouracil and nitrogen mustard, neither of which produced any beneficial effect. He returned to his home where he died in April 1958. A report from his family physician states that his terminal course was characterized by hepatomegaly, marked ascites, peripheral edema, and the development of subcutaneous nodules presumed to be metastases. Histologic confirmation of the nature of these nodules was not obtained, and roentgenographic study of the chest was not carried out. No postmortem examination was performed.

IATROGENIC DISSEMINATION OF NEOPLASTIC CELLS

The case reported above clearly represents an instance of iatrogenic dissemination of neoplastic cells. This distressing complication may occur in several ways:

1. Local wound implantation. The oldest and most commonly recognized form of recurrence

attributable to the surgical procedure is the development of tumor in the operative wound as the result of seeding of the exposed tissue with free tumor cells. The most frequent examples are probably noted following radical mastectomy or radical neck dissection but such implants may occur in any operative wound. The recent reports of Smith and co-workers[9] have confirmed previous reports of the presence of apparently viable tumor cells in washings taken from such wounds. Such implants will obviously be most frequent in operations for extensive tumors in which adequate margins cannot be obtained and where tumor bearing lymphatics or other tissues are transected. In such instances, thorough irrigation of the wound, preferably with some tumoricidal solution, will minimize the possibility of such an event. If dissemination by this means is to be eliminated, however, the performance of a careful *en bloc* dissection of the primary tumor and its regional nodes is essential. In those lesions which require biopsy prior to resection, care must be taken to avoid contamination of the definitive wound by instrument or glove-borne cells from the biopsy wound. Separate sets of instruments, new gloves and fresh wound drapes are mandatory if this preventable spread is to be avoided.

2. Intestinal suture-line implantation. Although basically a variation of the first category, this form of implantation is sufficiently important to merit individual consideration. Free tumor cells can regularly be demonstrated within the bowel lumen in tumors of the intestines, and the number of such cells is greatly increased by the unavoidable manipulation of the lesion consequent to removal. Implantation of these cells upon the freshly sutured intestinal wound is presumably responsible for suture-line recurrences in patients in whom adequate margins of normal tissue have been demonstrated histologically. Attempts to prevent the seeding of these cells have taken the form of preliminary ligation of the bowel at the proximal and distal limits of the proposed resection before manipulation of the tumor, and irrigation of the bowel lumen above and below with solutions presumably capable of destroying the free tumor cells. While these techniques are not completely effective, they should certainly be utilized for whatever measure of protection they offer.

3. Graft donor-site implantation. Operative procedures which require the use of free or pedicled skin grafts have resulted in the transfer of tumor cells to the donor site. There can be little doubt in such instances that contaminated gloves or instruments carried viable tumor cells to the fresh, open wound where conditions were favorable to survival and growth. The obvious remedy for this preventable dissemination is rigid and complete isolation of the separate fields.

4. Blood stream dissemination. The recent studies of Cole[8] have clearly demonstrated the striking increase in the number of tumor emboli present in the venous blood draining the tumor bearing area during the period of operative manipulation. Furthermore, Fisher and Fisher[4] have conclusively shown that such emboli may lie dormant for a period of time before developing into recognizable metastases. Although it seems certain that many such emboli do not survive to produce distant metastases, there can be no question that the probability of successful implantation of such emboli is increased in direct proportion to the number of cells disseminated by this means. Proximal ligation of the venous drainage prior to any manipulation of the tumor would appear to be of paramount importance in the operative removal of all neoplasms. The dissemination of tumor cells to distant sites as the result of failure to employ such preventive measures is as clearly the responsibility of the surgeon as if tumor cells had been deliberately implanted in those sites.

5. Intraperitoneal implantation. The mechanism with which this report is primarily concerned is the inadvertent seeding of the peritoneal serosal membranes with neoplastic cells at the time of operation. It is well recognized that these surfaces present a favorable environment for the implantation and growth of such cells. The development of serosal implants is a frequent event in the natural history of many intra-abdominal neoplasms. This event usually occurs late in the course of such tumors and is associated with penetration of the neoplasm through the serosa. Such penetration is accurately regarded as of serious prognostic significance even though obvious implants are not visible at the time of operation. The recent studies of Moore and his associates[6] with regard to the presence of free tumor cells in the peritoneal fluid in patients with intra-abdominal neoplasms confirm the validity of this impression.

These observations make it highly probable

that neoplastic cells dislodged from the primary tumor and seeded into the peritoneal cavity by the trauma of operative manipulation would find an environment highly favorable to their survival and growth. Suggestive evidence to substantiate this may be derived from those instances in which a tumor is ruptured during the process of removal. The incidence of peritoneal implants in these circumstances is understandably high. When obvious seeding does not occur, however, it is difficult to establish beyond doubt a causal relationship between the operative procedure and the subsequent development of peritoneal implants, since this event might have occurred spontaneously, the microscopic deposits of tumor being too minute to be grossly visible at the time of the procedure.

The case history herein reported is clearly an example of iatrogenic intraperitoneal dissemination of tumor. At the time of the original operation, the tumor in this patient was confined within the rectus sheath and did not involve the peritoneum. Contact with the peritoneal cavity was established only during operation when an incision was made through the peritoneum and posterior rectus sheath and the tumor incompletely removed across the peritoneal cavity. The subsequent course of this patient was marked by rapid and extensive local recurrence, and diffuse growth of tumor throughout the peritoneal cavity. These implants grew with great rapidity and eventually caused the death of the patient. It is extremely improbable that such diffuse peritoneal involvement could have occurred as the result of lymphatic or blood stream spread.

It is equally improbable that dissemination of the tumor cells occurred subsequent to the time of operation. After the initial incomplete resection, the tumor recurred locally and invaded the parietal peritoneum at the site of incision. It is conceivable that the diffuse implants developed from cells cast off from this local intraperitoneal invasion. The time sequence suggests, however, that this was not the case since only 3 months after the onset of recurrent symptoms, the peritoneal implants were found to measure up to 2.5 cm. in diameter. Furthermore, the implants were distributed uniformly throughout the abdominal cavity with no preponderance near the primary lesion. It is well recognized that intraperitoneal seeding is extremely atypical of this group of tumors even when peritoneal invasion is present. The predominant pattern of behavior is rather one of local invasion with an almost negligible tendency to metastasize to distant sites by any route. A search of the literature has failed to reveal an instance of diffuse seeding of the peritoneal cavity under any circumstances. In light of these observations, it seems virtually certain that dissemination took place at the time of the original operative procedure. Regardless of the exact timing, however, the iatrogenic nature of the spread is unaltered.

The complex set of events noted in this case is admittedly highly unusual but clearly establishes the possibility of intraperitoneal seeding of tumor at operation, proof of which is difficult to obtain under most circumstances. This observation, added to the circumstantial evidence noted above, suggests that this mechanism of dissemination is probably more important than is generally recognized. Microscopic serosal invasion and penetration by tumor cells is well known to exist more often than is suspected on gross inspection of the lesion at operation; the possibility of dissemination by this route is correspondingly greater than might be anticipated.

Several techniques may minimize the possibility of intraperitoneal dissemination of tumor:

1. Any exploration or operative procedure to be carried out in other regions of the peritoneal cavity should be accomplished before molesting the tumor.

2. The operative area should be partitioned from the general peritoneal cavity as effectively as possible by careful and adequate placement of laparotomy pads. This packing should be maintained throughout the procedure, and the pads should be removed from the table as soon as the resection has been completed.

3. The instruments utilized for resection of the tumor should be kept separate as though the area were bacteriologically contaminated and should not be used in the completion of the procedure.

4. Gloves should be changed and potentially contaminated wound drapes should be replaced following completion of the resection of the tumor.

5. Consideration should be given to the possibility of applying an occlusive envelope to the primary lesion as early in the procedure as possible. A significant amount of manipulation is unavoidable in the resection of most neo-

plastic lesions, and the possibility of dislodging tumor cells is inevitably present. Such wrapping should serve to minimize the intraperitoneal dissemination of neoplastic cells. The application of a tumoricidal or histotoxic solution to the tumor prior to wrapping would appear theoretically advantageous.

6. Irrigation of the local area with a tumoricidal solution following resection may be of value. A questionably valid objection to this procedure is the possibility of mechanically disseminating viable cells by this means. If the solution were sufficiently efficacious in destroying free cells, however, this objection would be overcome. Furthermore, the substance must not exhibit significant local toxicity for normal cells or serious systemic effects. Recent reports[3] suggest that monoxychlorosene (Chlorpactin XCB) may meet these requirements. Irrigation of the entire peritoneal cavity would appear to be indicated if a suitably effective solution were available.

It is the responsibility of the surgeon to recognize the mechanisms by which the inadvertent dissemination of neoplastic cells may occur and to utilize every means at his disposal to prevent such spread. Although it is obviously discouraging to the surgeon to know that his efforts to eradicate the primary tumor may be negated by the dissemination of neoplastic cells during the operative procedure itself, it is particularly distressing to realize that such an event might have been prevented.

ABDOMINAL WALL TUMORS

The case under discussion is of particular interest in view of the fact that the tumor in this patient arose in the musculofascial structures of the abdominal wall. In the past, lesions involving these structures have generally been considered to be predominantly benign in nature. This view has been based upon the belief that the most common tumor in this location is the so-called "desmoid tumor" and that this is a benign lesion. Our own observations indicate that neither of these impressions is correct. Classification of the desmoid tumor as a benign lesion is not compatible with its locally malignant behavior and its ability to cause the death of the

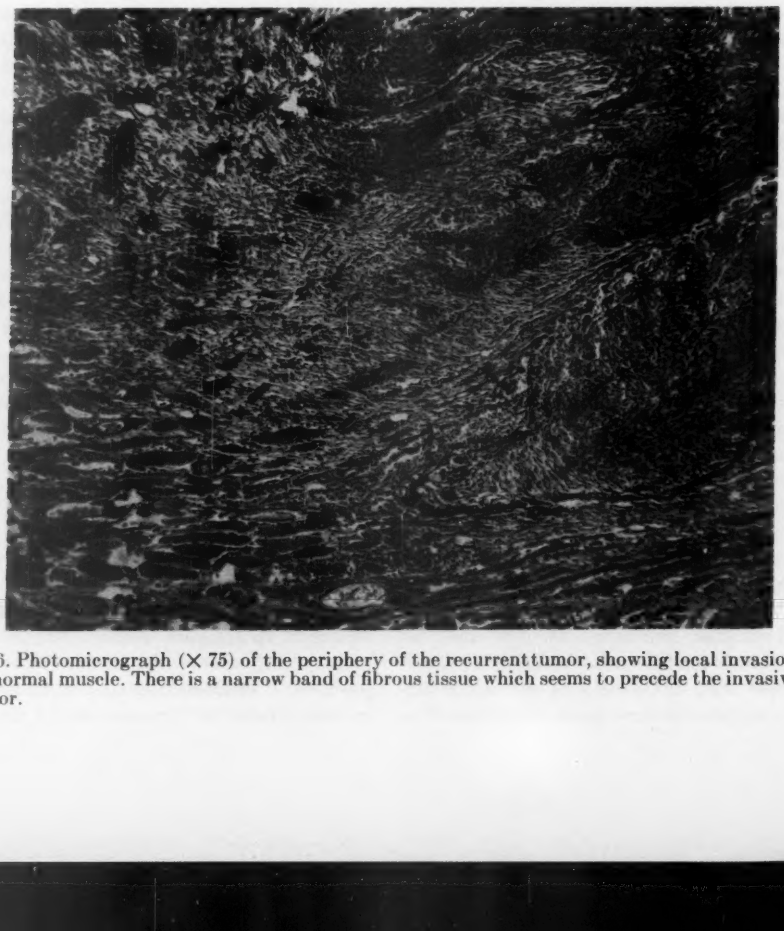

FIG. 6. Photomicrograph (× 75) of the periphery of the recurrent tumor, showing local invasion of adjacent normal muscle. There is a narrow band of fibrous tissue which seems to precede the invasive cellular tumor.

patient. This lesion should be classified as a well differentiated, low grade fibrosarcoma.[2]

If desmoid tumors are classified as malignant neoplasms, then the overwhelming majority of primary connective tissue tumors of the abdominal wall will be found to be malignant. Regardless of this consideration, however, a large proportion of such tumors will prove to be clearly defined fibrosarcomas. Approximately 45 per cent of our own cases have been unequivocally diagnosed as sarcoma, and 52 per cent of the abdominal wall tumors of musculofascial origin reported in Stout's series[10] of soft tissue sarcomas were classified as fibrosarcoma in contradistinction to desmoid tumors. These observations emphasize the fact that the benign attitude with which abdominal wall tumors have been regarded is entirely unjustified. There would appear to be an entire spectrum of connective tissue tumors of varying degrees of malignancy which may occur in this location, the lowest on the scale being the desmoid tumor, the highest being the very cellular, highly malignant fibrosarcoma. The tumor found in the presently reported patient is an example of the latter.

It is of clinical significance that this entire group of tumors appears to exhibit a behavior pattern in which local invasion (fig. 6) predominates whereas distant spread, either by lymphatics or blood stream, is rare. That this picture is characteristic of the low grade fibrosarcoma, or desmoid tumor, is well recognized, but it appears to be almost equally true of the more aggressive fibrosarcomas. The patient herein reported represents one of the few reported instances in which distant metastases developed. It must be stated that the evidence in this case is only presumptive since no biopsy of the reported subcutaneous nodules was obtained. Furthermore, the reported hepatomegaly cannot be unequivocally interpreted as being secondary to metastatic tumor. A chest film was negative 4 months before death. If these findings did, in fact, represent blood stream dissemination of tumor, this case is unique in this respect. The only other reported case of distant spread by such a tumor is that of Pack[7] who observed a patient in whom an abdominal wall fibrosarcoma spread to the inguinal lymph nodes. Stout reports 13 tumors of this type, none of which revealed distant metastases. In view of this significant tendency to remain localized, these tumors would seem particularly susceptible to surgical cure, and the possibility of iatrogenic dissemination becomes even more distressing.

Examples of transplantation of fibrosarcoma are rare. To our knowledge, the only unequivocal case reported in the literature is that of Harrell and Valk[5] in which a fibrosarcoma of the heel was accidentally transplanted to the site of a pedicled flap raised on the thigh. A probable but unproved case is that of Arnsperger[1] in which excision of a sarcoma of the ovary was followed by peritoneal implants. Since the originl tumor was intraperitoneal, however, the possibility of spontaneous seeding cannot be excluded. It is obvious that the possibility of intraperitoneal dissemination of sarcoma is small since the abdominal cavity will rarely be exposed. Abdominal wall tumors represent the most likely source of such dissemination. The more highly malignant fibrosarcomas are most apt to be transplanted. It is less likely that desmoid tumors will behave in this fashion since, in general, well differentiated tumors are less likely to survive transplantation. Nonetheless, neither the infrequency with which implantation has been reported nor the expectation that such an event is improbable in the case of low grade tumors should cause a relaxation of precautionary efforts to prevent this occurrence. The present case graphically demonstrates the possibility of iatrogenic spread and the unfortunate sequelae which may follow. Since the nature of the lesion cannot be known before biopsy, it is mandatory that all lesions of the abdominal wall be treated as though they were highly malignant until proved otherwise. An exact histologic diagnosis should be established by incisional biopsy and frozen or permanent section. Instruments used for biopsy should be discarded and the tumor excised with a wide margin of normal tissue, taking care to avoid violating the neoplasm during this procedure. If these precautions are followed, neither local recurrence nor dissemination should result and a high rate of permanent cure should be anticipated.

SUMMARY

1. Iatrogenic dissemination of neoplasms may occur by several mechanisms. A summary of these is presented.

2. Intraperitoneal dissemination is one such

mechanism. Although usually difficult to prove unequivocally, it is probably more frequent than realized. An undoubted instance of peritoneal seeding of a fibrosarcoma of the abdominal wall is presented.

3. Techniques which should minimize the possibility of dissemination of tumor during operation are presented. It is the responsibility of the surgeon to utilize every available means to prevent this distressing complication.

4. All tumors arising in the abdominal wall should be considered to be malignant until proved otherwise. The operative management of such lesions should be characterized by all the respect accorded any malignant neoplasm. Failure to follow this recommendation may result in the unfortunate sequelae noted in the patient herein reported.

5. Desmoid tumors should be classified as low grade, well differentiated fibrosarcomas and should be managed in accordance with the preceding principles.

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REFERENCES

1. Arnsperger, L.: Über Spätrecedive maligner Tumoren. Beitr. path. Anat., *Supp. 6-7:* 283, 1904.
2. Cantrell, J. R., and Riley, L. H., Jr.: The desmoid tumor: a malignant neoplasm. Submitted for publication.
3. Collier, R. G., Ey, R. C., McDonald, G. O., and Cole, W. H.: Wound irrigation to prevent local recurrence of cancer. A. M. A. Arch. Surg., *78:* 528, 1959.
4. Fisher, B., and Fisher, E. R.: Experimental studies of factors influencing hepatic metastases. III. Effect of surgical trauma with special reference to liver injury. Ann. Surg., *150:* 731, 1959.
5. Harrell, G. T., and Valk, A. de T.: Autogenous transplantation of a fibrosarcoma of skin during the application of a full-thickness skin graft. Ann. Surg., *111:* 285, 1940.
6. Moore, G. E., Burke, E., Skjorten, F., Badillo, J., and Kondo, T.: Appraisal of tumor cell spread into the abdominal cavity. Surg. Forum Am. Coll. Surg., 1959 (to be published).
7. Pack, G. T., and Ariel, I. M.: *Tumors of the Soft Somatic Tissues*, p. 266. Paul B. Hoeber, Inc., New York, 1958.
8. Roberts, S., Watne, A., McGrath, R., McGrew, E., and Cole, W. H.: Technique and results of isolation of cancer cells from the circulating blood. A. M. A. Arch. Surg., *76:* 334, 1958.
9. Smith, R. R., Thomas, L. B., and Hilberg, A. W.: Cancer cell contamination of operative wounds. Cancer, *11:* 53, 1958.
10. Stout, A. P.: Fibrosarcoma. The malignant tumor of fibroblasts. Cancer, *1:* 30, 1948.

A METHOD OF MARKING FOR THE SURGICAL SPECIMEN*

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A very essential and integral ingredient of any radical resection and continuity dissection for cancer is a painstaking and complete pathologic examination of the operative specimen. Multiple frozen section examinations, both from the margins of the primary tumor and various suspicious areas in the nodal area will give only a portion of the information desired. The slow, careful examination of the complete operative specimen is vital before all final conclusions can be reached.

The operative identification of the anatomical components of a specimen is often a tedious and impossible task at the completion of a lengthy operative procedure. The surgeon will usually attempt to "tag" the margins of the radical resection with sutures, baggage tags or slips of paper. These usually become lost in transit to the Pathology Department, and the specimen arrives without any orientation data for the pathologist.

The device herein described was planned in order to permit an immediate identification tag to be clipped to any portion of the specimen as the operation progresses. During the procedure, all pertinent anatomical sites can be quickly and indelibly tagged. The pathologist can be accurately oriented as to the anatomy, limits of dissection and the exact margins of the resection. A more helpful and much needed pathologic examination can then be done, and the operator is in a much better position to judge the adequacy of his resection.

Sterile metal tags of some sort are the natural solution. Small discs have been tried, but these had to be made to order and of necessity were quite expensive. Recently at the suggestion of Dr. Gabriel Tucker of The Johns Hopkins Hospital Otolaryngological Department, the Pilling Company was contacted as to the feasibility of numbering Michel skin clips consecutively. This turned out to be an ideal and inexpensive answer to the problem. The clips are supplied on racks of 25, numbered 1 through 25. When the surgeon encounters each new area that should be accurately identified, he applies

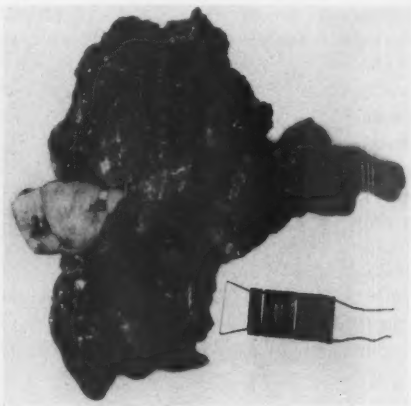

FIG. 1. Numbered Michel skin clips. Clips are visible attached to the specimen.

the next numbered clip, and the number with its proper anatomical index is written on the pathologic sheet immediately (fig. 1).

Comment. These clips to date have been used in several dozen head and neck composite resections. They have been enthusiastically accepted by the pathologists as a welcome addition to the procedure.

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THE CORRECTION OF DEFORMITY IN THE ADULT CLEFT PALATE PATIENT*

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Thousands of adults in this country today are still troubled by residual deformity after repair of cleft lip and palate in childhood. Some of these had surgery performed by the unskilled or inexperienced. Others had deformities of such severity that the finest surgical care in childhood still left them with undesirable stigmata.

Plastic surgery and our understanding of the meaning of deformity continue to progress. Many of these adults could now receive additional help for their appearance and speech. Physicians must be aware of the possibilities as a great deal of human suffering may be prevented by taking advantage of improvements in surgery.

This paper deals with a consideration of the treatment of the most obvious remaining deformity in the adult cleft palate patient—labionasal recession associated with underdevelopment of the upper jaw.

For the past 10 years plastic surgeons have focused more attention on ways to eliminate dangers to bone and soft tissue growth that might follow surgical correction of cleft lip and palate. Studies that were first reported included children with poorly developed maxillae from a variety of causes. These included some treated by bone-crushing techniques as advocated in the 1920's by Brophy, some with severe congenital hypoplasia of the entire central face[1], some in whom surgeons had injudiciously removed a premaxilla, and some with underdevelopment that *may* have resulted from reduction in blood supply to the growth centers in the central face. *It has not been established that simple elevation and mobilization of soft tissue from the underlying palate or maxilla will significantly reduce bone growth*, but some investigators[3, 5, 6] have found evidence that critical growth centers can be readily damaged by surgical manipulations of the bone itself. In children with double cleft lip it is clear that surgical manipulations of the premaxilla or even the septum immediately behind it may be followed by grave growth retardation of the middle face.[2] This premaxilla is separated in the normal newborn child from the bony septum by an area of cartilage showing marked proliferation of osteoblasts, but in the child with a congenital cleft this zone has much less osteoblastic activity. Thus, it may be seen *that many children with cleft lip and palate will have a marked lack of maxillary development even in the absence of any surgical manipulations.*[5, 6]

Certainly we shall continue to see children with recessed upper lips and small upper jaws

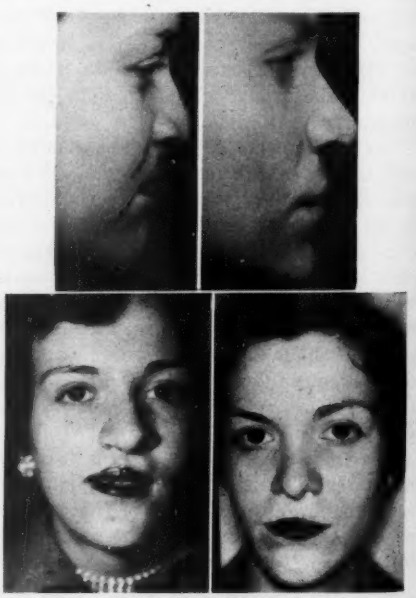

FIG. 1. (V. R., JHH #471179). This young woman, having had a standard type of repair of a double cleft lip deformity in infancy, was increasingly troubled by the "snarling expression" and flatness of the central face on profile. The views on the *left* show the preoperative conditions. The views on the *right* show the results of mobilization of the cheeks and lips forward with an advancement technique in the buccal sulcus.

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until the basic etiology of cleft lip and palate is uncovered—even if all children with cleft palates receive ideal atraumatic surgery, *i.e.*, surgery that does not add to the basic reduction in bone growth[4] (Fig. 1*A-B*).

The flat upper lip and protruding lower one are the main ingredients of the so-called "cleft palate facies." It is this flatness and disproportion of the face which may be seen at a distance of 50 yards that gives the cleft palate child a deep sense of deformity and ugliness at a very early age. It is more severe in the double cleft deformity, but also present with single clefts. Patients describe this tightness of the upper lip as giving them "a constant snarl" and point out that it is much more distasteful than the presence of surgical scars on the lip surface.

Physicians in general and even plastic surgeons have at times been slow to encourage patients with this "flat-face" deformity to seek plastic correction. There is an understandable reluctance to embark on a new major reconstructive procedure with an adolescent or young adult if he or she seems to have made a reasonable emotional adjustment to that deformity. However, repeatedly, I have felt rewarded by correction of this labionasal recession and would like to call attention to several means whereby it may be improved.

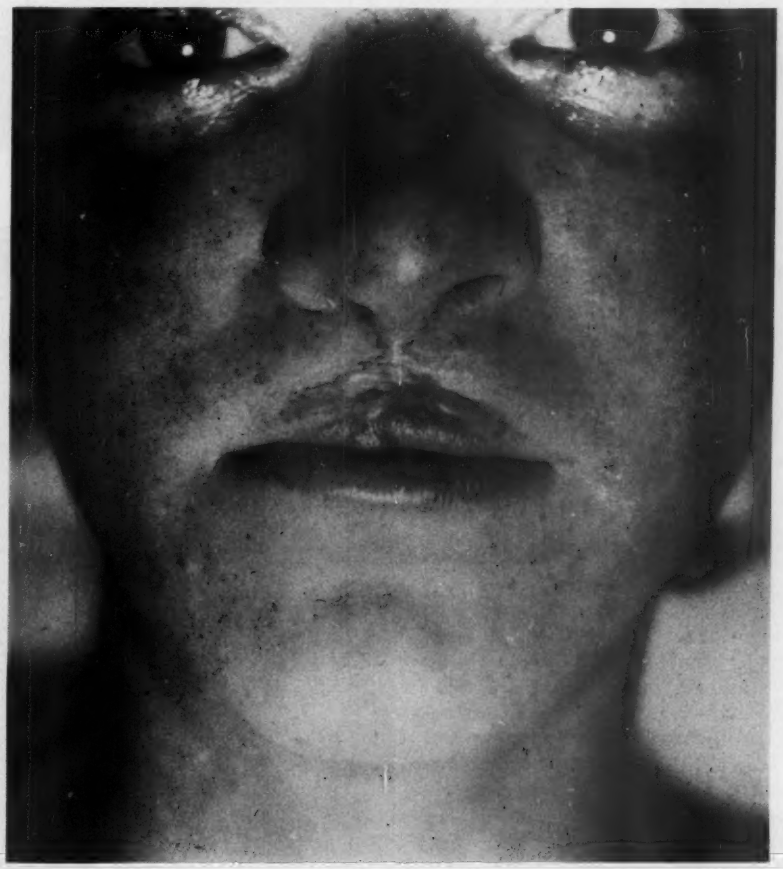

FIG. 2*A*. (V.R., JHH #471179). Patient is seen with a central midline scar resulting from closure of a double cleft lip in childhood.

FIG. 2*B*. Removal of scar with the insertion of a full thickness graft to recreate a philtrum

TREATMENT

When lip flatness is only moderate and the underlying maxilla is reasonably well developed, a great deal may be accomplished by mobilizing the cheeks forward with L-shaped incisions in the upper buccal sulcus. This tends to balance the relative redundancy of the lower lip. At the same time the columella of the nose may be lengthened to release the nasal tip from the lip (fig. 1).

Many times these patients will have a central or midline scar in the upper lip after repair of a double cleft in infancy. This can be converted to resemble a normal philtrum by replacing the scar with a full-thickness graft about 8 mm. wide (figs. 2*A* to 2*D*).

When the soft tissue defect of the upper lip is too severe for an advancement, a pleasing correction is often obtainable by use of an Abbé flap from the mid-portion of the lower lip to the upper (fig. 3). This has the added advantage of reducing the redundancy of the lower lip that resulted from constricting of the oral commissures at the time of original lip repair (figs. 7 *C* and 7*D*).

At times the mid-face has an acceptable amount of labial and nasal soft tissue but lacks sufficient skeletal support. On such occasions help may be offered in the form of bone grafting to lift the nasal tip upward, or, at times, additional bone or cartilage may be placed transversely in the lip to bring forward the recessed

FIG. 2C. Close-up of graft after healing

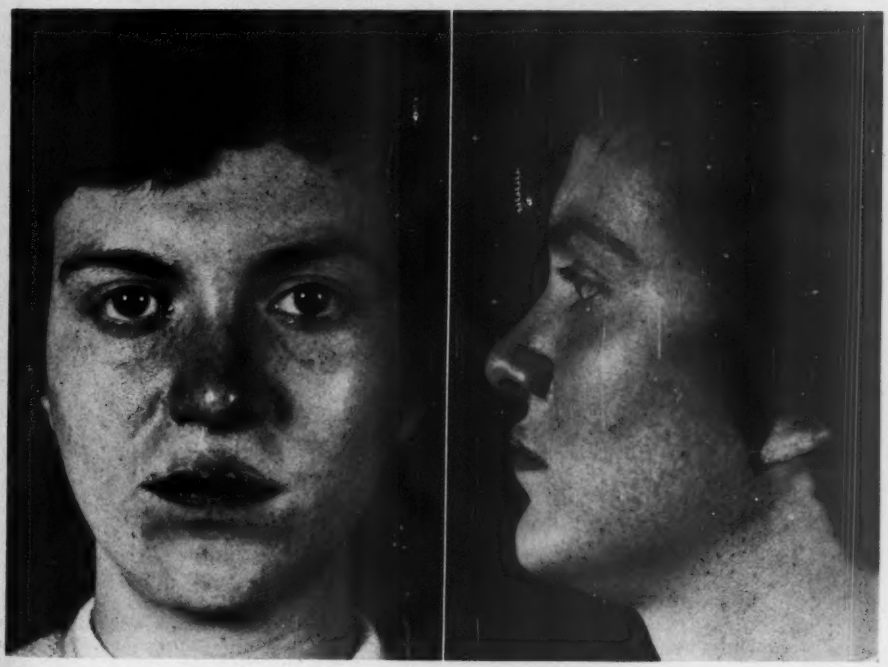

FIG. 2D. Profile and front views with final correction of recession in maxillary region. Facial balance is now satisfactory.

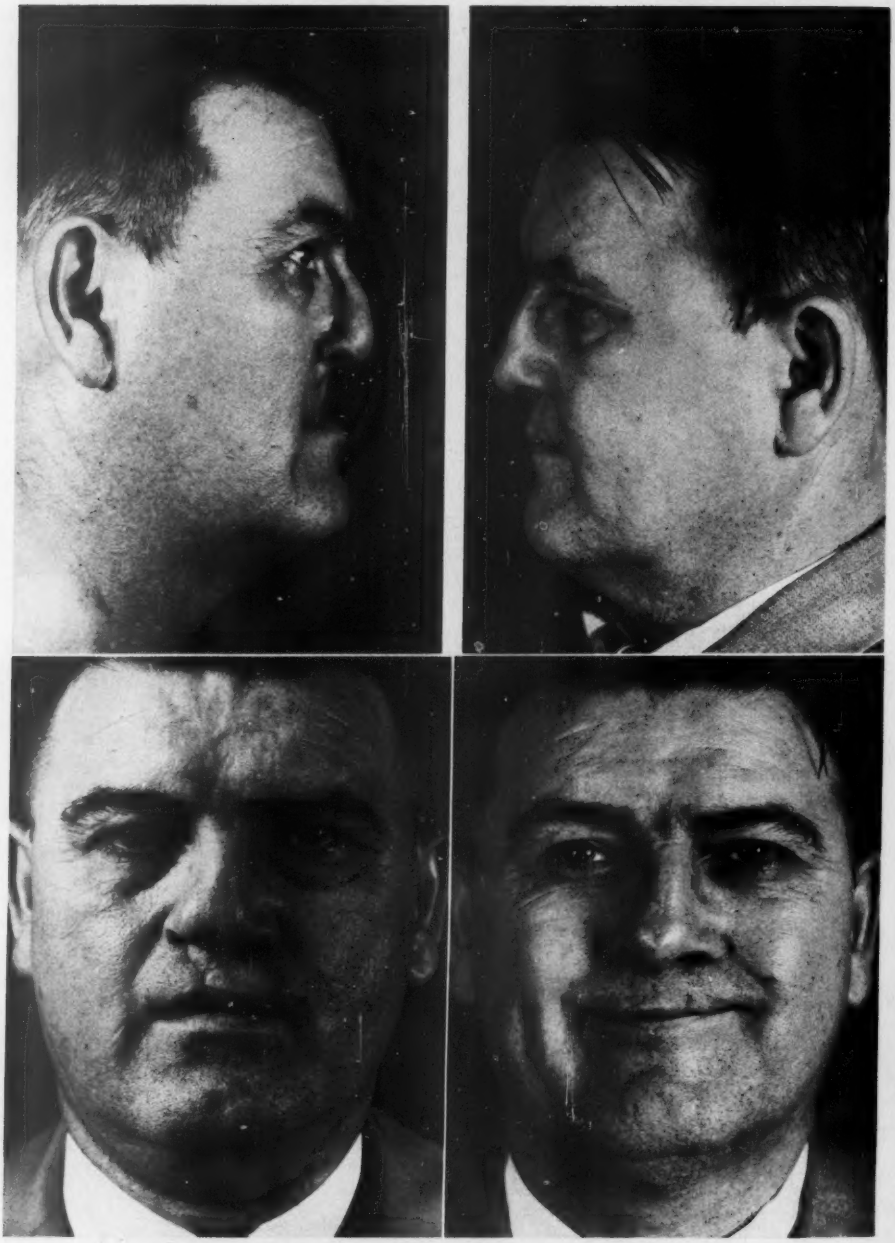

FIG. 3. (J. K., JHH #716276). This patient presented in adult life, having suffered from a deep "sense of ugliness" his entire previous life because of a "dish-face" deformity of his upper jaw. Profiles and front views show the tremendous effectiveness of an Abbé switch flap from the lower into the upper lip to relieve the facial disproportion. Many adults in this country could profit from this type of procedure. Pre-operative views are on the left and postoperative views are on the right.

nostril bases. In several patients we have used, with success, a polyvinyl-alcohol sponge to build up a depressed maxilla.

When the patient possesses a deficiency of mucous membrane behind the upper lip, as is often the case when the premaxilla has been removed in infancy, one may attempt to correct the labionasal recession by creating an enlarged lip sulcus with the aid of a skin graft and then utilize a dental prosthesis to supply both the missing teeth and the needed "filling out" of the central face (figs. 4*A* to 4*D*).

If a free skin graft cannot be used behind the upper lip to supply a sulcus without creating a large fistula into the floor of the nose, consideration should be given to the use of pedicle flap tissue. This may be conveniently supplied from the cervical region and used to close the fistula, supply bulk to the upper lip, and line the sulcus. If the patient needs lengthening of his palate to improve his speech, the tail end of this flap may be carried back and attached to the posterior pharyngeal wall for palate elongation (figs. 5A to 5*E*). We have used such tubes in

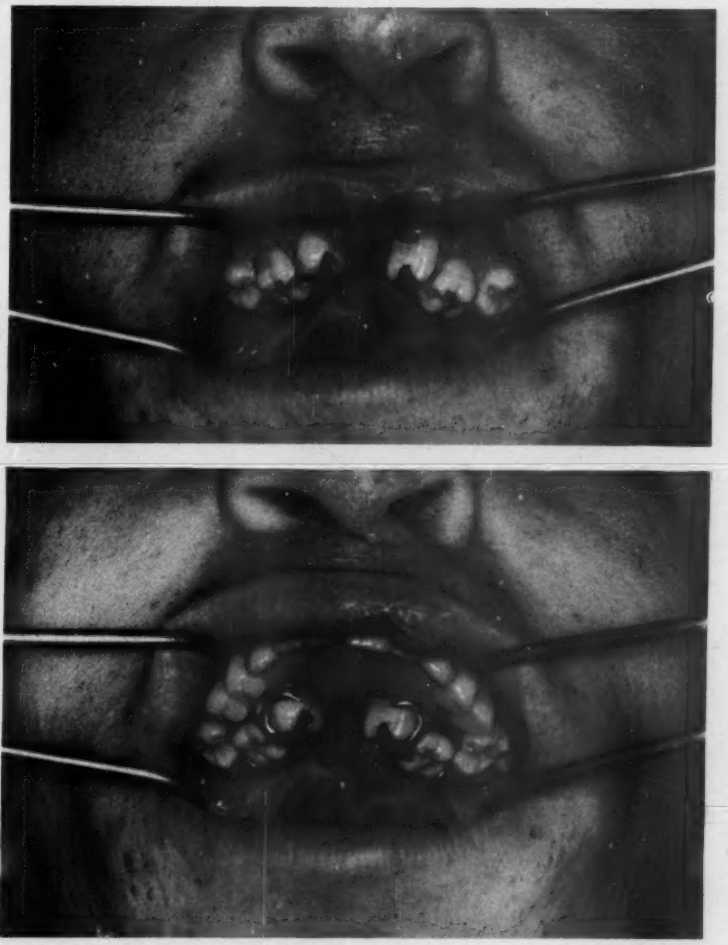

FIG. 4*A* (*top*). (T. P., JHH #612488). This young man is troubled by lack of maxillary development associated with a bone crushing type of surgery in infancy similar to the Brophy technique. *A* shows the marked constriction of the upper arch and its satisfactory correction (*B*, *bottom*), by the use of a large anterior dental prosthesis.

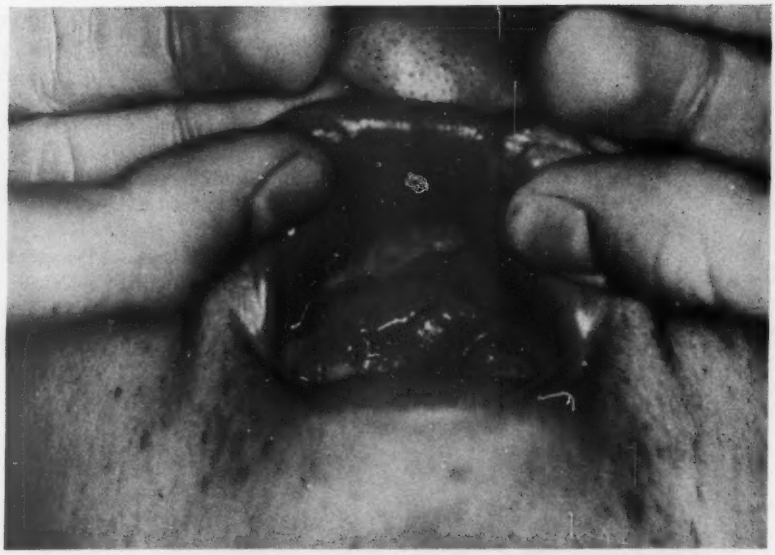

FIG. 4*C*. A portion of the skin graft used to line the upper sulcus and mobilize the lip and base of nose forward may be seen behind upper lip.

FIG. 4*D*. A comparison of the pre- and postoperative profiles after sulcus reconstruction and application of denture. Gratifying personality changes followed this plastic correction.

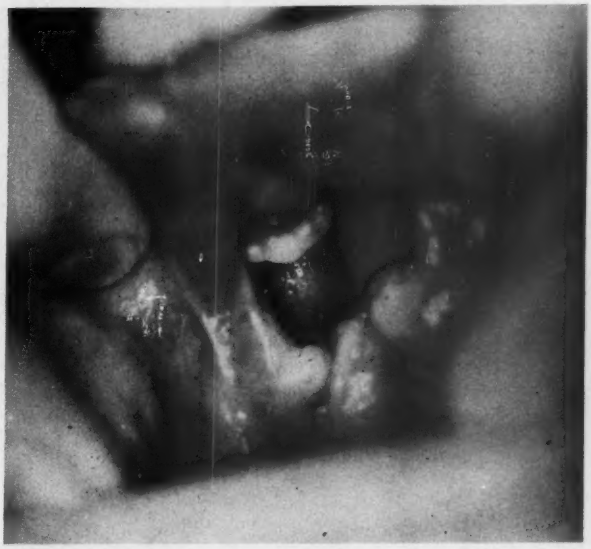

FIG. 5A. (J. K., JHH #716276). Fistula of anterior palate due to childhood removal of entire premaxilla. Underdevelopment of the entire middle face followed.

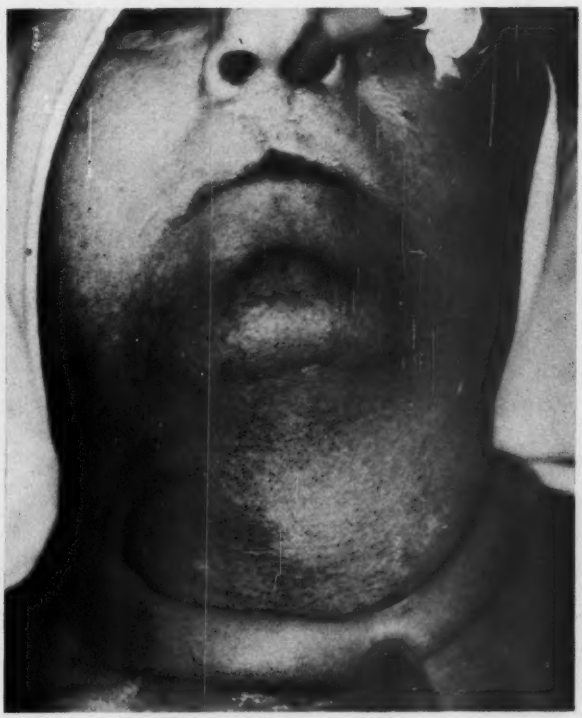

FIG. 5B. Construction of cervical neck tube

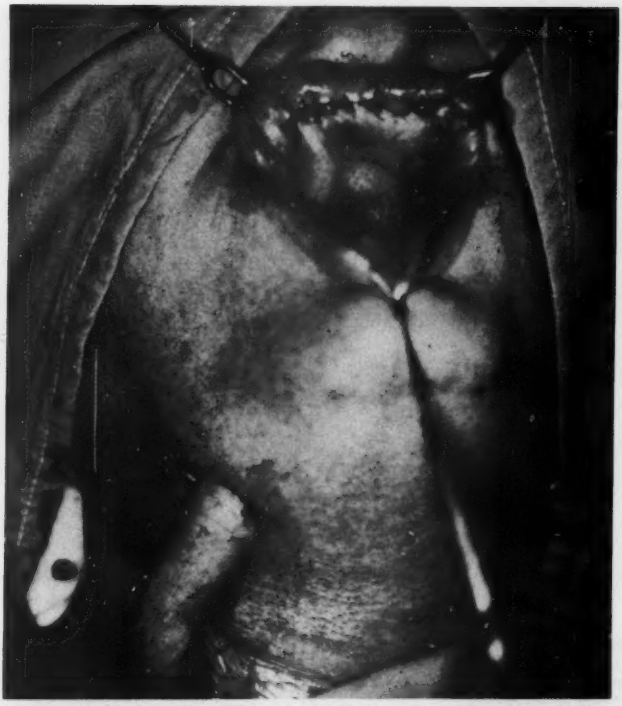

FIG. 5*C*. The transfer of one end of cervical neck tube by way of cervical incision into fistula behind upper lip

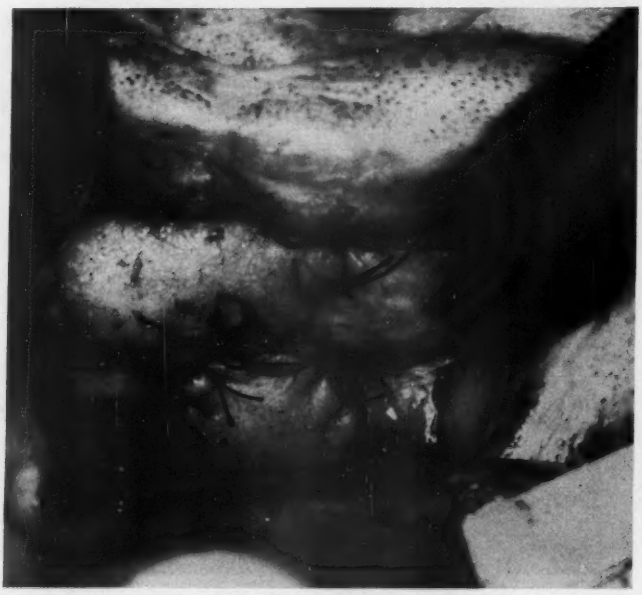

FIG. 5*D*. Flap in place to fill out area of maxillary underdevelopment and close fistula

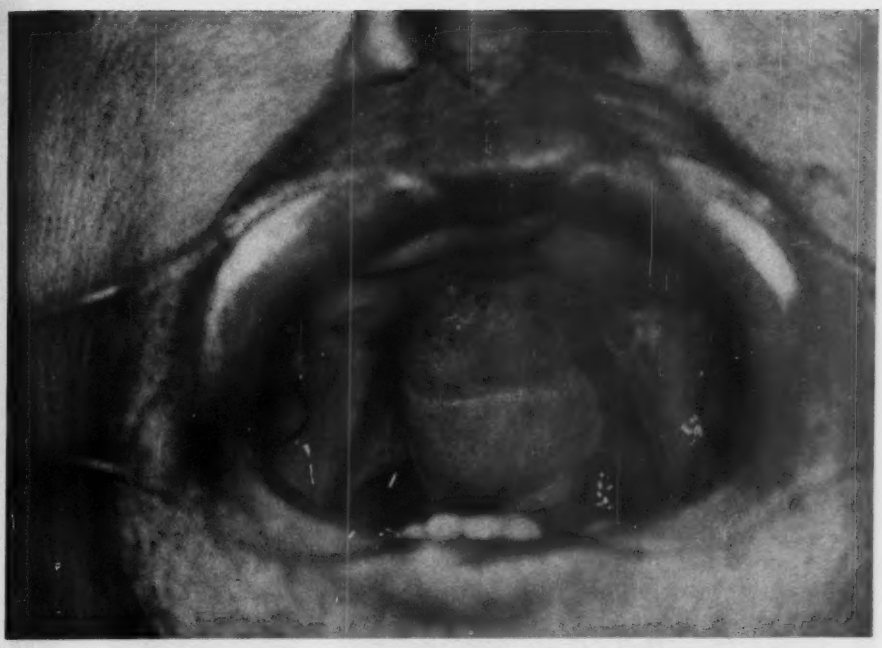

FIG. 5*E*. The opposite end of this flap was transferred into the soft palate and posterior pharynx to improve velopharyngeal closure. The appearance of the patient after surgery is illustrated in figure 3.

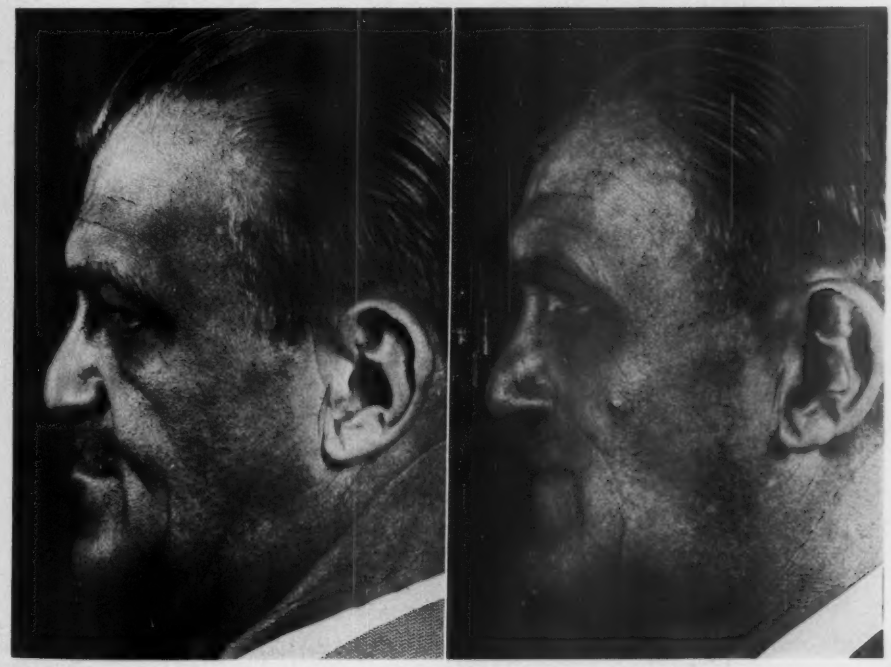

FIG. 6*A*. (C. O., JHH #361041). Preoperative and postoperative profiles of patient receiving excisions of large amounts of skin and subcutaneous tissue from the nasolabial fold on either side of the upper lip.

FIG. 6*B*. Pre- and postoperative front views of the same patient. Note improvement in facial relationship associated with changes in cheek regions.

FIG. 7*A*. (R. L., JHH #746032). Patient with double cleft lip deformity repaired in childhood by surgical technique involving a direct attack on the region of the premaxilla. Nasolabial recession developed. Correction of the bulky nasal tip by direct removal of skin and cartilage is outlined on illustration.

FIG. 7*B*. The actual removal of nasal tissue at the time of operation

FIG. 7*C*. The pre- and postoperative profiles show effect of reduction of nasal bulkiness in association with an Abbe switch flap from the lower into the upper lip. Striking rehabilitation of this patient resulted from these corrections.

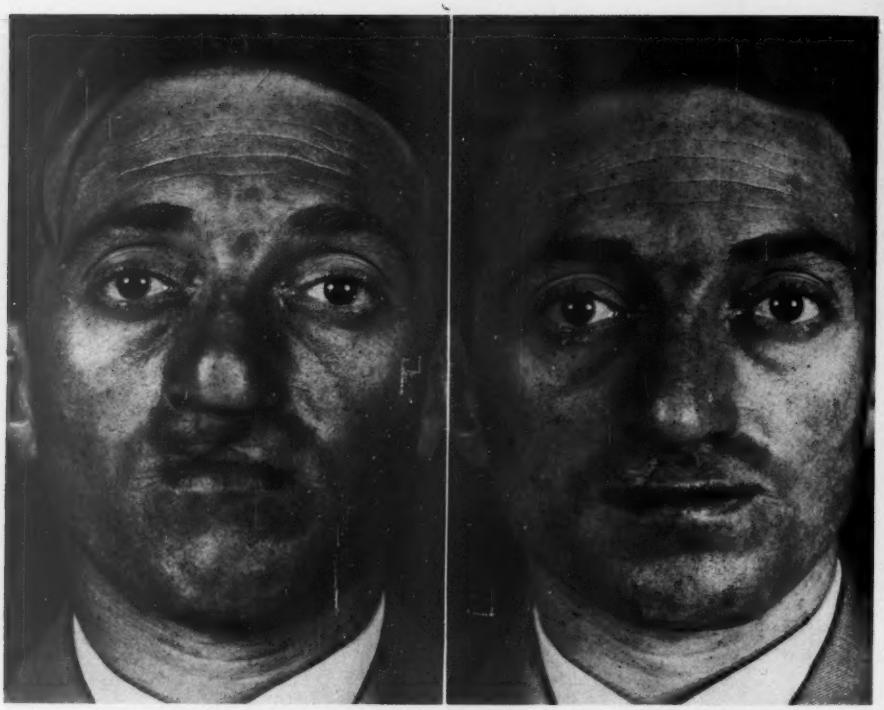

FIG. 7*D*. The pre- and postoperative front views after surgery to tip of nose and Abbé flap from lower lip.

three patients to reconstruct the soft palate and posterior pharynx with marked improvement in speech in each.

These various maneuvers to overcome labionasal recession may further be supplemented by work on the adjacent features to establish facial harmony. I have already mentioned the desirability of removing a full thickness wedge from the redundant lower lip in many cases. To this we should add consideration of excising the heavy nasolabial cheek folds—particularly in the adult or older patients (figs. 6*A* and 6*B*). This has the effect of bringing the upper lip forward and markedly improves the breathing in many instances.

The nose of the double cleft lip patient is quite characteristic. It is wide at the tip and short in length. The columella is very short and tends to pull the tip downward into the so-called "porcine" deformity. This is made more unsightly by the high flared positions of the alae with deficient bulk and hence exposure of too much nasal vestibule. It is not within the scope of this paper to describe the many ways to correct this nasal deformity, but the nasolabial recession due to underdevelopment of the maxilla may be greatly helped by direct reduction of bulk in the nasal tip (figs. 7*A* to 7*D*) and by advancement of alar bases with reduction in the circumference of the nasal apertures.

Many of the above procedures have been described by previous writers and used at times with great skill. Some of the techniques we believe to be new. Certainly there has been insufficient emphasis on the potential help that may be given the adult cleft palate patient who finds his facial image the cause of unhappiness, withdrawal, self-consciousness, and social ineffectiveness. Most of these people can be given a reasonably normal appearance and find the effort most worthwhile.

SUMMARY

Thousands of adults in this country have unsightly results from repair of cleft lip and palate. These results are partly a result of surgical

trauma, but also are related to congenital defects in growth centers of the middle face. Labionasal recession associated with maxillary underdevelopment is the most common deformity contributing to the "cleft palate facies."

Plastic surgery now has available many techniques for the correction of these deformities. The choice of the proper procedures for restoring facial balance and improved speech will yield highly rewarding results for both the surgeon and his patient.

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REFERENCES

1. Avery, J. K., and Devine, R. K.: Development of ossification centers in the face and palate of normal and cleft palate human embryos. Cleft Palate Bulletin *9:* #2, 25, 1959.
2. Beder, O. E., Carrell, J., Coe, H. E., and Moore, A. W.: The problem of the premaxilla in bilateral cleft lip and cleft palate. Oral Surg., *12:* 156, 1958.
3. Cronin, T. D.: Surgery of the double cleft lip and protruding premaxilla. Plast. & Reconstruct. Surg., *19:* 389, 1957.
4. Marcks, K. M., Trevaskis, A. E., Payne, M. J., and Kicos, J. E.: The management of the secondary cleft lip deformities. Am. J. Surg., *95:* 932, 1958.
5. Monroe, C. W.: The surgical factors influencing bone growth in the middle third of the upper jaw in cleft palate. Plast. & Reconstruct. Surg., *24:* 481, 1959.
6. Slaughter, W. B., and Brodie, A. G.: Facial clefts and their surgical management in view of recent research. Plast. & Reconstruct. Surg., *4:* 311, 1949.

DUODENAL DIVERTICULUM: CLINICAL SIGNIFICANCE AND SURGICAL TREATMENT*

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Sir William Osler[15] first described primary diverticulum of the duodenum in the American literature in 1881, but the first recorded case is that of Chomel[5] in 1710. By 1951, a direct surgical attack upon a duodenal diverticulum had been carried out by Key and Forssell,[9] the diagnosis having been established by fluoroscopic examination. Nevertheless, the clinical significance of the disease tends to remain obscure. Such symptoms as have been ascribed to it are largely nonspecific, suggesting the possibility of functional disorder, or are not to be readily differentiated from those due to coexistent disease.

There are only two presentations in the American literature which discuss surgical therapy in relatively large series. Cattell and Mudge[2] in 1952 described the experience at the Lahey Clinic with 25 patients. In 1955 Waugh and Johnston[18] discussed the surgical treatment of 30 patients at the Mayo Clinic. Each group demonstrated a mortality rate of 7 to 8 per cent. This hazard involved in surgical treatment provoked grave doubts as to the advisability of operation. In an attempt to resolve this problem the experience at the Johns Hopkins Hospital is presented.

This study of the cases of primary duodenal diverticulum seen at the Johns Hopkins Hospital during a 23-year period to October 1959, represents an effort to appraise the symptomatology and to assess the use of operation. The group under study is comprised of 90 cases in which the disease was demonstrated by x-ray. Thirty-two of these patients were submitted to operation because of their symptoms.

SYMPTOMATOLOGY

The symptoms encountered in the group of patients seen at the Johns Hopkins Hospital are outlined in table 1. It is immediately apparent that in the group suffering from duodenal diverticula and free from concomitant disease, upper abdominal pain, nausea, dyspepsia and diarrhea occur with an important frequency, affecting roughly 50 per cent or more of the victims. Diarrhea occurred with an especially great frequency.

In the presence of concomitant disease diarrhea was much less often seen as a presenting symptom. However, the significance of the symptoms here becomes more difficult to evaluate. Table 2 lists the concomitant diagnoses in the 56 cases of this group. It will be noted that colon disease, biliary tract disease, and hiatus hernia are the most prominent of the organic diseases in this list. Inferentially one may reach two conclusions with regard to the symptoms in the group with other disease (table 1). First, the most common symptoms do not help in specifying the causative disease. Second, a lesser symptom might lend weight to one or another diagnosis.

The majority of persons with duodenal diverticulum may well suffer no ill effect. However, when the appearance of symptoms has prompted radiographic examination of the upper abdomen, the disclosure of a duodenal diverticulum cannot be dismissed. One may choose to attribute symptoms to intermittent obstruction of the diverticulum, to stasis, or to duodenitis. It must be conceded in any event that the appearance of the common symptoms in the group of patients with duodenal diverticulum alone would indicate strongly that a causal relationship exists.

In 1949 Chamberlain[3] discussed his case and reviewed the literature applying to this disease. Although he stressed the variability of the symptoms, his review indicates that the recent studies antedating his report began to demonstrate certain consistencies of symptomatology.

Mahorner's report[12] emphasized the appearance of diarrhea. In the Lahey Clinic report of Cattell and Mudge[2] 12 patients had duodenal diverticulum as the sole disease. Of these 12, 11 suffered

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TABLE 1

Frequency of symptoms in 90 patients with demonstrated duodenal diverticula

Symptom	Duodenal Diverticulum Alone (34 Cases)		Duodenal Diverticulum and Other Disease (56 Cases)	
	Number	Percentage of group	Number	Percentage of group
Diarrhea	24	71	11	20
Upper abdominal pain	22	64	35	62
Nausea and/or vomiting (epigastric distress, flatulence)	18	51	25	45
Dyspepsia (eructation, belching, and/or distention)	17	50	39	70
Hematemesis; melena	11	32	6	11
Fever	1	3	3	5

TABLE 2

*Concomitant diagnosis in 56 of 90 patients with duodenal diverticulosis**

Diagnosis	Patients	
	Number	Percentage of 90
Diverticulosis coli	22	26
Hiatus hernia	17	18
Biliary tract disease	16	18
Peptic ulceration	4	4
Portal cirrhosis	3	3
Pancreatic tumor	3	3
Pancreatic	3	3
Jejunal diverticulum	3	3
Meckel's diverticulum	2	2
Esophageal diverticulum	1	1

* Only demonstrated organic disease is tabulated.

upper abdominal pain, 6 were flatulent, 4 had nausea and vomiting, and 5 experienced weight loss. Only Chitambar[4] takes exception to the prominence of diarrhea as a symptom. Of Woodruff's 3 patients, 2 suffered epigastric pain.[19] Hilton[10] treated 5 patients who were symptomatic. All had epigastric pain, 3 had vomiting and nausea, 2 had weight loss. Elstner and Waugh[7] discussed the problem in 1957. Pain, dyspepsia, nausea, weight loss, jaundice and diarrhea were the predominant symptoms.

The graver symptoms of bleeding, manifested as hematemesis or melena, occurred in approximately one-third of our patients with duodenal diverticulum alone. Forrest[8] has recently discussed this complication. The jaundice due to peri-Vaterian location is also well known.[11]

One may conclude, therefore, that the duodenal diverticulum may underlie a syndrome of epigastric pain, dyspepsia, nausea and diarrhea. It may less frequently be the source of upper gastrointestinal bleeding or jaundice. The appearance of these symptoms in the patient who can be demonstrated to have no other lesion compels one to accept the diverticulum as the culpable disease. Where concomitant disease exists one may be unable to specify as to cause of these symptoms, but the view that the diverticulum is an unlikely source is erroneous. Substantiation for these views is to be found in the consistency of the reports from many authors and from the figures presented in this report.

SURGICAL THERAPY

Our experience with surgical intervention when duodenal diverticulum was present is categorized in table 3. Thirty-two patients underwent exploratory laparotomy because of symptoms which might be attributed to the diverticulum according to the criteria set forth above. In each instance the lesion had been demonstrated by roentgenographic study before operation. To permit comparison, the patients are presented in five categories which divide them according to the presence or absence of concurrent disease, and according to whether or not the diverticulum was treated. Patients were followed no less than one year. They were considered well if the symptoms leading to treatment had disappeared and had not returned.

Table 3*A* indicates that when the diverticulum was apparently the sole lesion responsible for the symptoms, resection cured 5 of 8 patients. Table 3*B* adds 1 patient to the group of cures where the surgical attack was to bypass the diverticulum. In 4 patients, the lesion remained untreated, and these patients remained unimproved, as shown in table 3*C*.

The existence of concurrent disease would appear to pose a problem in evaluating cure. Table 3*E* illustrates the results in 12 patients who had

TABLE 3

The results of surgery in patients with duodenal diverticulum

	Well	Not Well
A. Eight patient with duodenal diverticulum as sole disease in whom diverticulum was resected or inverted		
195622	×	
334489		Died
449468	×	
489560	×	
496082		×
498964	×	
578364		×
559014	×	
B. One patient with duodenal diverticulum as sole disease in whom diverticulum was bypassed		
127397	×	
C. Four patients with duodenal diverticulum as sole disease in whom diverticulum was untreated at operation		
170652		×
482720		×
497353		×
447753		×
D. Seven patients with duodenal diverticulum and other disease in whom the diverticulum was resected		
166205 (peptic ulcer)	×	
417589 (hiatal hernia; diverticulum inverted)	×	
452926 (gall bladder disease)	×	
480841 (diverticulosis coli)		×
492232 (cholecystitis)	×	
515724 (hiatal hernia)	×	
848944 (hiatal hernia and pancreatitis)		Died
E. Twelve patients with duodenal diverticulum and other disease in whom the diverticulum was untreated at operation		
386542 (cholecystitis)		×
470459 (hiatal hernia)		×
471657 (diverticulosis coli)		×
477372 (gall bladder disease, pancreatitis)		×
493882 (gastric ulcer)		×
497006 (gall bladder disease)		×
534998 (hiatal hernia: gall bladder disease)		×
557842 (hiatal hernia)		×
562555 (cholecystitis)		×
563884 (peptic ulcer)		×
577933 (pancreatic cyst)		×
588869 (gall bladder disease)		×

duodenal diverticulum as well as another lesion. The diverticulum was left untreated in these patients. Nine of the 12 patients had a surgical procedure directed to the correction of the other disease. In 3 patients only exploration was carried out. In no instance was the patient rendered well.

Conversely, table 3*D* illustrates the experience when the diverticulum was treated in the presence of other disease. Of this group of 7 patients, 6 were treated for both diseases, 1 for the diverticulum alone. Of 7 patients 5 were cured of their symptoms.

Stated grossly, table 3, *A*, *B* and *E*, shows that when diverticulum was present and treated, 11 of 16 patients were relieved of the symptoms for which operation was performed; 3 were unrelieved; 2 patients died. When duodenal diverticulum was present and left untreated 16 of our 16 patients remained ill, whether or not a concurrent disease was treated.

If one attempts to reduce these figures to percentages, to permit comparison, it may be stated that in this series, 6 of 9 patients or 67 per cent of patients who had resection or bypass for duodenal diverticulum uncomplicated by the presence of other disease experienced good results. This figure compares closely with the figure of 50 per cent stated from the Mayo Clinic[18] and 53 per cent from the Lahey Clinic.[2]

This experience is reinforced by the apparent benefit derived by patients with coexistent disease when the duodenal diverticulum is treated as well as the other disease. Of 7 such patients (71 per cent) 5 had good results. There was striking contrast with the group with concurrent disease where the duodenal diverticulum was untreated (table 3*D*). Failures to relieve symptoms resulted.

Patterson and Bromberg[16] summarized their views regarding the patient with diverticulum and coexistent disease "... in those cases where

surgery has been performed for symptoms supposedly or truly arising from some associated lesion the continued presence of a duodenal diverticulum left untouched can be a haunting spectre if and when symptoms do recur." Ackermann[1] and Pearse[17] suggested that this untreated diverticulum might be culpable in certain cases of postoperative cholecystectomy syndrome. Our figures demonstrate that in 8 cases of the 19 patients with coexistent disease, gall bladder disease was the accompanying illness. In the 6 instances where cholecystectomy alone was carried out, no cure ensued. In the remaining 2, where diverticulectomy was carried out with cholecystectomy, therapy was successful.

Our data lend credence to the view that in the presence of symptoms, the untreated diverticulum will defeat the surgical effort, whereas the opposite will apply for the majority of patients whose diverticula are treated.

THE RISK OF SURGICAL THERAPY

Two of our patients died as a result of their operations:

Case 1 (#334489). A 48-year-old white man was admitted to the hospital on October 14, 1944. He had a history of dyspepsia and postprandial pain and vomiting of many years duration increasing in severity during the 2 years preceding admission. Six months before admission he had massive hematemeses on two occasions. Physical examination revealed epigastric tenderness as the only abnormal finding. Roentgenographic examination of the upper gastrointestinal tract disclosed the presence of several duodenal diverticula, with an irregularity of the mucosal pattern of one suggestive of an inflammatory process. No duodenal ulcer was seen.

The patient's pain was not relieved by medical management. On October 26, 1944, an exploratory laparotomy was carried out. One duodenal diverticulum was resected after dissection from the pancreas. The common duct was found to enter the dome of a second diverticulum. This was partially resected and a rubber tube inserted into the duct and ampulla to support the repair. Fifteen hours after the operation was over the patient's temperature rose to 105°. It remained at this level. The patient's blood pressure fell to levels of 80/60 within 5 hours, and he did not respond to vigorous supportive measures. Bile drained from the wound during this period. Thirty-six hours after operation, jaundice appeared and the patient became anemic. Death supervened 42 hours after operation.

Postmortem examination revealed hemorrhagic pancreatitis and peritonitis.

Case 2 (#848944). A 48-year-old white woman was first admitted on June 4, 1959, with a complaint of abdominal pain of 2 years' duration. The patient had undergone appendectomy and salpingectomy in 1939. Two cesarian sections were carried out in 1931 and 1933. In 1949 a cholecystectomy was performed, and in 1957 intestinal adhesions were lysed. During the year preceding admission the patient had had upper abdominal pain with increasing frequency. This was aggravated by a high alcoholic intake for one year. Two weeks before admission the patient had been admitted to another hospital with acute, severe, abdominal pain, which was demonstrated to be due to an acute pancreatitis.

Laboratory studies revealed a normal hematocrit and leukocyte count, normal liver function studies, normal serum amylase. Gastrointestinal x-ray studies revealed a hiatus hernia and duodenal diverticulum. In view of the recent attack of pancreatitis and the possibility of emotional overlay, the patient was discharged pending further evaluation.

The patient's symptoms of upper abdominal pain increased markedly and she was readmitted on August 10, 1959. The serum amylase was again normal. On August 11, 1959, laparotomy was carried out, with repair of hiatus hernia and resection of duodenal diverticulum. The diverticulum was deep in the pancreatic head, seemed inflamed and was first identified transduodenally. Within 12 hours of operation the patient's temperature rose to 105° and her serum amylase rose to 1860 units from 240 units preoperatively. This had risen to 3590 units, and the patient was in shock despite vigorous supportive therapy over the next 24 hours. The fulminant pancreatitis persisted, cardiac arrest supervened. Despite resuscitation, the patient succumbed on August 15, 1959.

Postmortem examination revealed pancreatitis, duodenitis and peritonitis.

One other patient suffered a duodenal fistula for six months but eventually recovered.

Case 3 (#952926). A 57-year-old man was admitted to the hospital on March 1, 1948, with a history of colicky pains in the upper abdomen for 4 years. Two months before admission he had suffered a severe hematemesis requiring hospitalization. Physical examination revealed right upper quadrant tenderness. Roentgenographic studies showed a duodenal diverticulum. There was no function of the gall bladder.

At operation on March 11, 1958, cholecystec-

tomy, common duct exploration and duodenal diverticulectomy were carried out. The diverticulum was approached anteriorly, traversing the pancrease. On the day after operation the patient's temperature rose to 104° and he showed signs of circulatory collapse. Copious drainage of bile appeared from the wound. The patient was felt to have atelectasis from which he recovered rapidly. However, biliary drainage of striking degree persisted for 2 weeks and was presumed to be due to a duodenal fistula. Approximately 3 months later the patient drained a small amount from the same site. He remained well, however, and was completely free of the abdominal complaints which he had endured prior to his operation.

Of our 16 patients, therefore, in whom the duodenal diverticulum was resected, 3 suffered major catastrophe. The series cited from the Mayo Clinic[18] discloses death in 2 instances of a series of 17 resections, 1 patient dying of pancreatitis and the other with a fistula. Cattell and Mudge[2] report two deaths in the group of 24 patients in whom resection was carried out at the Lahey Clinic.

This forbidding percentage of mortality would seem to be a strong deterrent to the extension of surgical therapy in any condition which did not pose a threat to life

Consideration of the patients who died in our group and in the two other series alluded to reveals certain striking common features. Of the 6 patients 4 died of fulminant pancreatitis. Our patient in this category suffered pancreatitis antedating her surgery. Indeed, this was such a prominent feature of her disease that it had served as a deterrent to surgery on an earlier admission (case 2). In another of these cases, a portion of the pancreas had been resected with the diverticulum.

A second group of patients succumbed with complications apparently involving the biliary tree. Case 1 proved to have a diverticulum around the ampulla of Vater and common duct intubation with repair about the catheter followed the surgery to the diverticulum. Two other patients underwent transplantation of the common duct and eventually died, as cited in these other series.

In summary, it would appear that common duct surgery or injury accompanying diverticulectomy augers ill for the outcome, that recent or concurrent pancreatitis may be a contraindication to excision, and that pancreatic resection should be avoided. Bypass of the affected area in such selected instances might well be the procedure of choice. It is conceivable that the mortality and serious morbidity from resection of duodenal diverticulum might be reduced to acceptable levels by more careful selection of patient and appropriate procedure.

DISCUSSION AND CONCLUSIONS

There can be no doubt that the overwhelming number of duodenal diverticula are so benign in their behavior as to obviate any necessity for considering their removal or treatment. Of those which are symptomatic, a number are apparently brought under perfectly acceptable control by simple medical measures constructed about bland diet and antacid regimens. A small group through such dangerous complications as hemorrhage, or because of troublesome symptoms refractory to medical measures are considered for surgical intervention.

A syndrome of upper abdominal pain, nausea, dyspepsia, and diarrhea presented itself in the majority of our patients with duodenal diverticulum uncomplicated by other gastrointestinal disease. The frequent coexistence of other disease of the gastrointestinal tract (62 per cent in our series) has made it difficult to assess the role of the diverticulum in these cases. Nevertheless, it may be said that the experience in cases with diverticulum alone demonstrates that this lesion may indeed produce symptoms.

Morton,[13] and Patterson and Bromberg[16] have felt that a large majority of symptomatic patients could be cured by surgery. Cattell and Mudge,[2] and Waugh and Johnston[18] have inclined to a less optomistic view, feeling that only some 50 per cent of patients operated upon would be benefited. In the series reported here, surgery directed toward the diverticulum was carried out in 16 patients, with benefit to 11 or 68 per cent.

Our study of those patients with duodenal diverticulum and symptoms attributable to the gastrointestinal tract, in whom surgery was not directed to the diverticulum, revealed a succession of disappointing results.

The mortality rate in the group undergoing surgical extirpation was 12 per cent (2 deaths) as compared with a similar rate reported from the Mayo and a rate of 8 per cent reported by Cattell from the Lahey Clinic. Pancreatitis and the necessity for common duct transplant because of the relationship of duct and diverticulum figures prominently in these catastrophies.

Ogilvie[14] has emphasized the role of the diverticulum in certain instances of pancreatitis. Hoffman[11] has reported the same. This may specifically have been the situation in one of our cases (I. D., #848944) which eventuated fatally. The pancreatitis in another case may have been provoked in the actual resection of pancreatic tissue. That the diverticulum around the ampulla of Vater, or the diverticulum into which the common duct opens directly poses a much more formidable problem in surgical resection is indisputable. Four of the 6 deaths tabulated above occurred in such cases. If discretion is to prevail, preoperative demonstration of this anatomical situation might incline the surgeon to consider bypass rather than resectional therapy. The technique described by Collett and his co-workers[6] whereby a barium demonstration of the diverticulum is synchronized with demonstration of the common duct by intravenous cholangiography affords a means of anticipating this relationship.

The experience of this clinic, weighed in the light of the reported experiences of others, had fostered certain conclusions with regard to the surgical aspects of the treatment of duodenal diverticulum. It becomes apparent that coexistent disease does not justify dismissal of duodenal diverticulum as a symptom-producing entity. Failure to recognize this is a frequent source of frustration to the surgeon and discomfiture to the patient. Surgical attack upon the diverticulum will afford relief of diarrhea, nausea, upper abdominal pain, or dyspepsia to the majority of patients. The appreciable mortality can be reduced by avoiding resection in the presence of pancreatitis, recent or recurrent, by avoiding pancreatic resection, or by avoiding resection involving the common duct. In these cases, bypass with or without gastric resection is best employed. It is tempting to conjecture that such an approach will at once lower mortality rates and also improve over-all cure rates.

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REFERENCES

1. Ackermann, W.: Diverticula and variations of duodenum. Ann. Surg., *117:* 403, 1943.
2. Cattell, R. B., and Mudge, T. J.: Surgical significance of duodenal diverticula. New England J. Med., *246:* 317, 1952.
3. Chamberlain, D.: Duodenal diverticula. Brit. J. Surg., *37:* 83, 1949.
4. Chitambar, I. A.: Duodenal diverticula. Surgery, *33:* 768, 1953.
5. Chomel, J. B. L.: *Histoire de l'Academie Royale.* Paris, 1710.
6. Collett, H. S., Tirman, W. S., and Caylor, H. D.: Roentgen demonstration of the common duct entering a duodenal diverticulum. Radiology, *55:* 72, 1950.
7. Elstner, H. L., and Waugh, J. M.: Duodenal and jejunal diverticula. Surgery, *41:* 674, 1957.
8. Forrest, A. B.: Incidence of bleeding in duodenal diverticula. Gastroenterology, *33:* 800, 1957.
9. Forssell, G., and Key, E.: Ein Divertikel an der Pars Descendens Duodeni mittels Roentgenuntersuchung Diagnostiziert und Operative Entfernt, Fortschr. Geb. d. Roentgenstrahlen, *24:* 48, 1916.
10. Hilton, H. D.: Primary duodenal diverticulum. Am. J. Surg., *87:* 259, 1954.
11. Hoffman, E.: Acute pancreatitis due to a peri-Vaterine. A. M. A. Arch. Surg., *78:* 177, 1959.
12. Mahorner, H.: Diverticula of duodenum. Ann. Surg., *133:* 697, 1951.
13. Morton, J. J.: The surgical treatment of primary duodenal diverticula. Surgery, *8:* 265, 1940.
14. Ogilvie, R. F.: Duodenal diverticula and their complications with particular reference to acute pancreatic necrosis. Brit. J. Surg., *28:* 362, 1941.
15. Osler, W.: Notes on intestinal diverticula. Ann. Anat. & Surg., *4:* 202, 1881.
16. Patterson, R. H., and Bromberg, B.: Surgical significance of duodenal diverticula. Ann. Surg., *134:* 834, 1951.
17. Pearse, H. E.: Surgical management of duodenal diverticula. Surgery, *15:* 705, 1944.
18. Waugh, J. M., and Johnston, E. V.: Primary diverticula of the duodenum. Ann. Surg., *14:* 193, 1955.
19. Woodruff, R.: Indications for surgical treatment of duodenal diverticulum. Am. Surgeon, *20:* 595, 1954.

THE HORMONE TREATMENT OF ADVANCED BREAST CANCER: COMPARATIVE THERAPY WITH TESTOSTERONE AND TWO EXPERIMENTAL ANDROGENS*

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In the treatment of *advanced* breast cancer the probability that we may ultimately fail in our efforts must not deter us from providing each qatient with the best possible program of palliative therapy. It has now been more than 70 years since Schinzinger,[7] in 1889, first suggested that surgical castration could be a practical therapeutic procedure in patients with breast cancer. Shortly after this, Beatson,[1] in 1896, reported the beneficial results of oophorectomy in patients with inoperable or metastatic breast cancer.

More recently it has been conclusively shown that major alterations in the endocrine environment of patients with advanced breast cancer can result in regressive changes in either the primary tumor or its more distant dissemination. However, these responses, dramatic as they occasionally may be, occur only in a minority of patients and are time limited in duration.

During the past 10 or 15 years many new and potent hormone preparations have become available which have allowed appreciable progress in this field of cancer chemotherapy. The concept of hormone therapy is based upon the fact that normal breast tissue is, at least, partially hormone responsive. Experimental evidence indicates that the growth of breast cancer is probably dependent upon the same hormones that are known to be responsible for breast development at puberty or breast hypertrophy at pregnancy. These hormones are secreted primarily by the anterior pituitary and the ovary and are aided perhaps, secondarily, by the adrenal cortex.

In 1937 Lacassagne[4] reported the use of androgens in the prevention of mammary cancer in mice, and in 1939 Loeser[6] reported encouraging clinical results in 2 patients with recurrent breast cancer treated with testosterone propionate. At present the sex hormones have a well deserved and recognized role in the palliative treatment of advanced breast cancer. Although many androgenic hormones have been used in the treatment of inoperable or metastatic breast cancer, none has thus far proved to be better than testosterone propionate in its antitumor effect. However, among the analogs of testosterone, the synthetic 2-methyl derivative of 4,5-α-dihydrotestosterone, has been reported recently by Blackburn[3] to be equal if not superior to testosterone.

The purpose of the present study is to compare the clinical effectiveness of three separate androgens (fig. 1) in the treatment of advanced breast cancer. These compounds are testosterone propionate and the oral androgen, testosterone, 9-α-fluoro-11-keto-17 methyl, in a comparison of primary hormone treatment, and 2-methyl dihydrotestosterone propionate in a comparison of secondary hormone treatment.

MATERIALS AND METHODS

Three series of postmenopausal patients with inoperable, recurrent or metastatic breast cancer all of whom showed convincing evidence of objective progression of their disease were carefully observed and treated in this study. The first series of patients receiving testosterone and the second series of patients receiving testosterone, 9-α-fluoro-11-keto-17 methyl were considered the *primary* hormone treatment group because none of these patients had received prior treatment with the sex steroids. All of the above patients were treated at the Breast Clinic of The Johns Hopkins Hospital in a program of "Cooperative Study to Evaluate Experimental Steroids in the Therapy of Advanced Breast Cancer" sponsored by the Cancer Chemotherapy National Service Center. The third series of patients receiving 2-methyl dihydrotestosterone, were dissimilar in that for the most part they were the private patients of one of us (E. F. L.) and had run the gamut of previous hormone therapy, and several had had endocrine ablation

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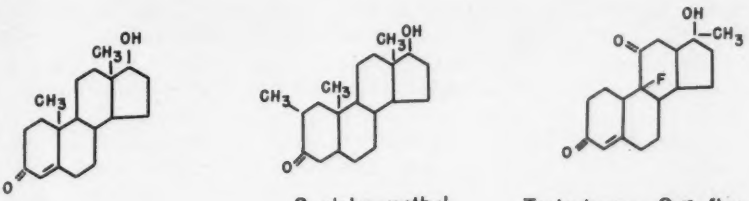
This study is published with the approval of the Cooperative Breast Group of the Cancer Chemotherapy National Service Center.



Testosterone

4-Androstene-3-one, 17β-hydroxy

2-alpha-methyl Dihydrotestosterone

2α-Methyl androstan-17β-ol, 3-one

Testosterone, 9α-fluoro-11-keto-17 methyl

4-Androstene-3,11-dione, 9α-fluoro-17β hydroxy-17α-methyl

FIG. 1. Chemical structure of androgens used in this study

TABLE 1

Results of primary hormone treatment and distribution of patients according to menopausal age

Menopausal Age*	Testosterone Propionate		Total	Testosterone, 9α-Fluoro-11-keto-17 Methyl		Total
	Progression	Regression		Progression	Regression	
<1 year	3	0	3	2	2	4
1-5 years	4	1	5	2	0	2
6-10 years	1	1	2	1	1	2
More than 10 years	7	4	11	11	1	12
Total	15	6	21	16	4	20

* Time since last menstrual period.

TABLE 2

Results of primary hormone treatment according to site of dominant lesion

Site of Lesion	Testosteroue Propionate		Total	Testosterone, 9α-Fluoro-11-keto-17 Methyl		Total
	Progression	Regression		Progression	Regression	
Breast, skin and lymph nodes	3	4	7	5	1	6
Bone	4	2	6	4	1	5
Visceral (lung, liver, brain)	8	0	8	7	2	9
Total	15	6	21	16	4	20

procedures as well. They were, therefore, considered the *secondary* hormone treatment group.

Patients in the first and third series received testosterone and 2-methyl dihydrotestosterone intramuscularly as its propionate ester in a dose of 100 mg. three times a week. Testosterone, 9-α-fluoro-11-keto-17 methyl was given orally in a dose of 40 mg. daily to patients in the second series. Follow-up observation was performed regularly once a month or more often if indicated, and all patients received treatment for an adequate period of time. X-ray examinations, laboratory studies and caliper measurements of accessible lesions were made at frequent intervals.

A total of 55 patients was included in the three series of this study. In the *primary* hormone treatment group there were 21 patients who received the reference standard testosterone propionate, and 20 patients who received the experimental androgen, testosterone, 9-α-fluoro-11-keto-17 methyl. In the *secondary* hormone treatment group there were 14 patients who received a therapeutic trial with 2-methyl dihydrotestosterone propionate.

In the *primary* hormone treatment group the patients were randomized in accord with their menopausal age (table 1) and in accord with the site of the dominant lesion (table 2). Thus, the patients in the first two series were selected with no individual bias and were as closely comparable as possible regarding prognosis. This, of course, was not the case in the third series of patients.

Patients having multiple sites of metastases were recorded as having their dominant lesion in the following order of precedence: (1) visceral, (2) bone and (3) breast, skin and lymph nodes.

The objective response of the primary tumor or its metastases was the *sole* criterion by which the clinical effectiveness of the androgen was evaluated. Subjective response was noted but was not regarded as critical for this study. Rigid criteria of objective regression were strictly adhered to, and briefly, these consisted of demonstrable improvement or diminution in size of at least 50 per cent of the total lesions whereas the rest remained unchanged. Progression of any lesion during treatment, or the appearance of new lesions usually precluded the possibility of regression.

TABLE 3

Results of hormone treatment

Treatment	Progression	Regression		Total
		No.	%	
Primary hormone therapy				
Testosterone propionate..	15	6	29	21
Testosterone, 9α-fluoro-11-keto-17 methyl.....	16	4	20	20
Secondary hormone therapy				
Testosterone, 2-α-methyl dihydrotestosterone....	12	2	14	14

RESULTS

Primary Hormone Treatment

There were 21 patients treated with testosterone propionate. Progression occurred in 15 (71 per cent), and regression occurred in 6 (29 per cent) as shown in table 3. There were 20 patients treated with the oral androgen, testosterone, 9-α-fluoro-11-keto-17 methyl. Progression occurred in 16 (80 per cent), and regression occurred in 4 (20 per cent).

A single observation indicating unequivoca

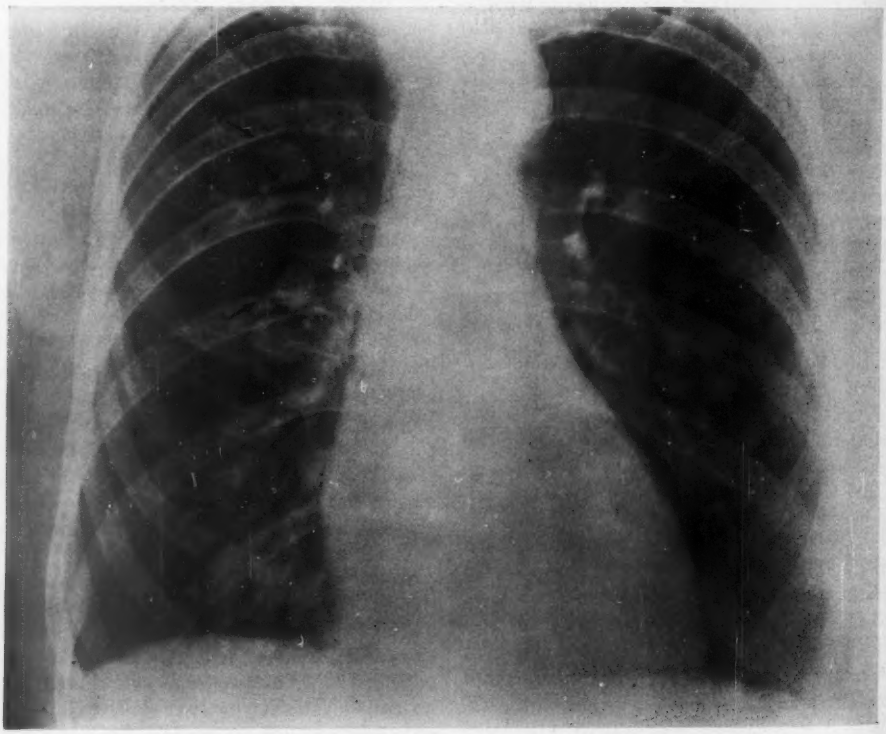


FIG. 2. Multiple pulmonary metastases before hormone treatment

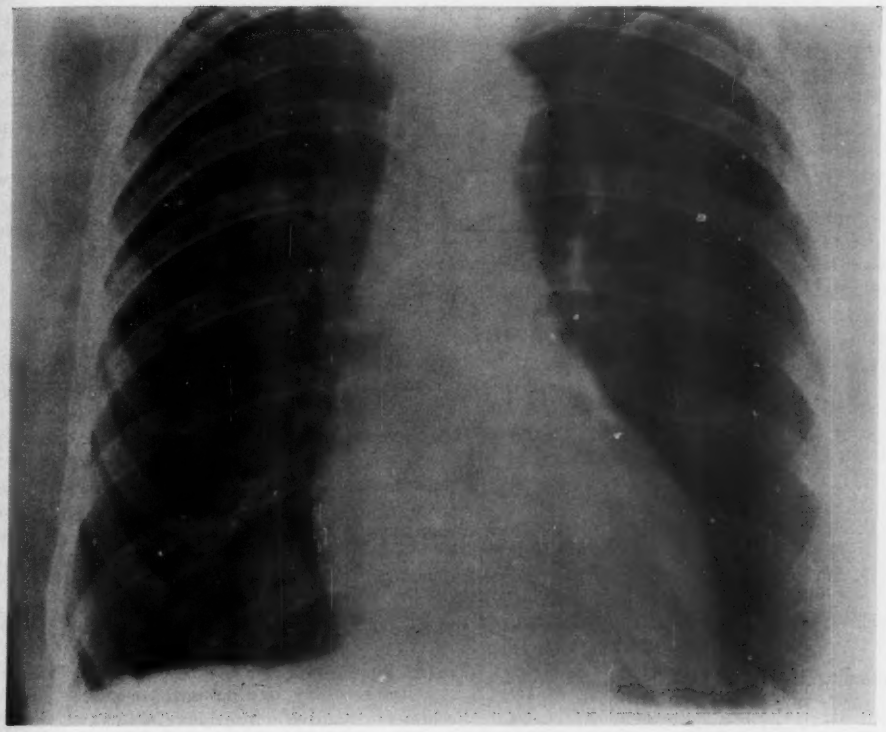


FIG. 3. Regression in both the size and number of pulmonary metastases after treatment with the oral experimental androgen.

objective regression was sufficient to classify the patient as having a favorable result (figs. 2 and 3). However, in those patients responding favorably to testosterone the average period of regression lasted 6.3 months, and in those patients responding to testosterone, 9-α-fluoro-11-keto-17 methyl the average period regression lasted 7.7 months.

The subjective response to hormone therapy was evaluated on the basis of relief of pain and a sense of well being. Since the power of "hope" in a "hopeless" disease is formidable, it is well to be extremely cautious in the interpretation of subjective improvement. Individual enthusiasm can often warp sound judgment. As noted previously by Lewison and his associates[5] most patients receiving testosteron experience euphoria and some degree of relief of pain. This subjective response is present regardless of the nature of the objective response. A comparable degree of subjective improvement was *not* noted in those patients receiving testosterone, 9-α-fluoro-11-keto-17 methyl. The virilizing effects varied individually with each patient, yet the hirsutism, deepening of the voice, and increase in libido were considerably more noticeable in the testosterone treated patients than in those treated with the experimental androgen.

Secondary Hormone Treatment

There were 14 patients treated secondarily with 2-methyl dihydrotestosterone. Progression occurred in 12 (86 per cent), and regression occurred in 2 (14 per cent) as shown in table 4. The 2 patients having a favorable response to this androgen had bone metastases as their dominant lesion; both had responded previously to castration therapy.

All patients in this series received treatment for between 4 and 26 weeks. There appeared to be little or no correlation in those patients showing progression between their objective result

TABLE 4

Summary of 14 patients treated secondarily with 2-α-methyl dihydrotestosterone

Patient	Age	L.M.P.*	Dominant Lesion	Duration of Therapy	Objective Clinical Result	End Result	Remarks
				wks.			
M. V.	58	1950	Visceral	10	Progression	Dead	Previous hormone therapy; no response
O. K.	51	1949	Breast nodes	8	Progression	Dead	Previous hormone therapy and hypophysectomy; no response
B. T.	50	1957	Visceral	10	Progression	Alive	Previous hormone therapy followed by hypophysectomy; minimal response
L. R.	55	1950	Bone	11	Progression	Alive	Previous hormone therapy followed by hypophysectomy; moderate response
R. B.	52	1949	Visceral	26	Progression	Alive	Previous hormone therapy; minimal response
C. D.	34	1959	Nodes	4	Progression	Dead	No previous hormone therapy; castration and x-ray therapy
V. D.	37	1955	Bone	25	Progression	Alive	Previous hormone therapy; moderate response
D. A.	64	1949	Bone	4	Progression	Dead	Previous hormone therapy; good response
E. W.	38	1959	Bone	9	Regression	Alive	No previous hormone therapy; castration
A. S.	64	1947	Bone	21	Progression	Dead	Previous hormone therapy; minimal response
M. R.	65	1927	Breast	20	Progression	Alive	Previous hormone therapy; minimal response
G. K.	45	1959	Bone	16	Regression	Alive	Previous hormone therapy and castration; moderate response
C. M.	41	1956	Bone	21	Progression	Dead	Previous hormone therapy; no response
E. N.	71	1941	Breast skin	6	Progression	Dead	Previous hormone therapy; good response

* Last menstrual period.

and their response to previous hormone treatment or endocrine ablation procedures.

Subjectively 2-methyl dihydrotestosterone had few if any toxic effects. It provided the patients with a good sense of well being and freedom from pain, and it appeared to have a low incidence of virilizing effects.

DISCUSSION

The results of this study indicated that testosterone propionate was more effective than either of the two experimental androgens with which it was compared. However, in those patients receiving secondary hormone treatment with 2-methyl dihydrotestosterone it is important to recognize that this selected series was dissimilar and not comparable to the primary hormone treatment group. These differences were accentuated by the fact that the cancer was considerably more advanced by the time secondary hormone therapy was initiated. It is also generally conceded that the chances of success decrease with each subsequent course of hormone therapy. As reported recently by our cooperative breast cancer study group of the Cancer Chemotherapy National Service Center, the regression rate is considerably lower for secondary hormone therapy than for primary hormone therapy.

In the testosterone treated patients it is interesting to note that the older the patient, the better the chance for a favorable result. This is consistent with similar studies of advanced breast cancer treated with either androgens or estrogens. Of a total of 11 patients who were more than 10 years past their menopause (table 1), there were 4 patients (36 per cent) who had an objective regression of their disease. The same was not true for testosterone, 9-α-fluoro-11-keto-17 methyl where 2 of the 4 patients showing objective regression were in the younger age group.

The prognostic significance of the dominant lesion was demonstrated by table 2. In the testosterone-treated patients objective regression occurred in 4 out of 7 patients when the dominant lesion was "breast, skin or lymph nodes," in only 2 out of 6 patients when the dominant lesion was "bone" and in 0 out of 8 patients when there was "visceral" involvement. This relationship did not appear to be as striking for those patients receiving the oral androgen.

The experimental androgen, testosterone, 9-α-fluoro-11-keto-17 methyl, used in this study is an analog of fluoxymesterone (Halotestin) which has recently been reported by Beckett and Brennan[2] as showing an objective regression rate of about 25 per cent.

SUMMARY AND CONCLUSIONS

1. Three series of postmenopausal patients with inoperable, recurrent or metastatic breast cancer were treated with testosterone propionate, testosterone, 9-α-fluoro-11-keto-17 methyl and 2-methyl dihydrotestosterone propionate. The first two series consisted of patients receiving *primary* hormone treatment, and the last series consisted of patients receiving *secondary* hormone treatment.

2. Objective regression occurred in 6 out of 21 testosterone treated patients (29 per cent) and in 4 out of 20 testosterone, 9-α-fluoro-11-keto-17 methyl treated patients (20 per cent).

3. Objective regression occurred in 2 out of 14 patients (14 per cent) treated secondarily with 2-methyl dihydrotestosterone.

4. In a carefully considered regimen of palliative therapy for patients with advanced breast cancer the androgens offer a good opportunity for both subjective and objective benefit.

Acknowledgments. The cooperation and assistance of the Cancer Chemotherapy National Service Center Staff is gratefully acknowledged.

The experimental hormones used in this study were prepared by Syntex, S. A. Mexico (2-methyl dihydrotestosterone propionate) and the Upjohn Company, Kalamazoo, Michigan (testosterone, 9-α-fluoro-11-keto-17 methyl).

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REFERENCES

1. Beatson, G. T.: On treatment of inoperable cases of carcinoma of the mammae: suggestions for new method of treatment, with illustrative cases. Lancet, *2:* 104, 162, 1896.
2. Beckett, V. L., and Brennan, M. J.: Treatment of advanced breast cancer with fluoxymesterone (Halotestin). Surg. Gynec. & Obst., *109:* 235, 1959.
3. Blackburn, C. M., and Childs, D. S., Jr.: Use of 2 alpha-methyl androstan-17 beta-ol, 3-one(2-methyl dihydrotestosterone) in the treatment of advanced cancer of the breast. Proc. Staff Meet. Mayo Clin., *34:* 113, 1959.
4. Lacassagne, A.: Relation between hormones and cancer. Canad. M. A. J., *37:* 112, 1937.
5. Lewison, E. F., Trimble, F. H., and Ganelin, R. S.: Advanced mammary cancer treated with sex hormones. J. A. M. A., *162:* 1429, 1956.
6. Loeser, A. A.: Male hormone in the treatment of cancer. Acta Union internat. contra cancrum, *4:* 375, 1939.
7. Schinzinger, A.: Centralbl. f. Chir. *16*, 55, 1889. Quoted by G. W. Taylor, and I. T. Nathanson in *Endocrinology of Neoplastic Disease.* Oxford University Press, New York, 1947. Also, Das Karzinom der mamma. Munchen. med. Wchnschr., *52:* 1724, 1905.

THE DIFFERENTIAL DIAGNOSIS OF EARLY JAUNDICE*

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The primary diagnostic problem in the patient with jaundice is the differentiation between hepatocellular and obstructive disease. Despite the frequently repeated statement that the jaundiced patient is not a surgical emergency,[2-4] optimal therapy demands the elucidation of the underlying cause of jaundice as quickly as possible. Unnecessary procrastination in operating upon the patient in whom obstruction exists will be to the patient's detriment.

Particularly perplexing are those patients who present immediately after the sudden onset of jaundice. The records of all such patients who were seen at The Johns Hopkins Hospital in 1952 and 1953 have been reviewed in an attempt to clarify this problem. This period was chosen for study in order to allow a 5-year period of follow-up for confirmation of the final diagnosis.

CLINICAL MATERIAL

Thirty-five patients who were seen after the acute onset of jaundice were studied. Those patients who had a history of icterus, blood dyscrasia, previous biliary surgery, or known toxic or infectious contact were excluded from this study. The age of the patients ranged from 26 to 60 years. There were 20 men and 15 women. Every patient was observed in the hospital for a minimum of 2 weeks and was followed for at least 5 years. In 24 patients, a tentative diagnosis of infectious hepatitis was made at the time of admission, whereas extrahepatic disease was suspected in 11 patients. Of the 11 patients who were considered on the basis of their initial studies to have obstructive disease 2 died early in the course of hospitalization. At autopsy, both had cholelithiasis without evidence of parenchymal liver disease, and jaundice was considered to be secondary to choledocholithiasis. Death in both instances was due to myocardial infarction. In all other patients in this group, the diagnosis of extrahepatic obstruction was confirmed by laparotomy.

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The 35 patients have been divided into 2 groups depending upon whether the jaundice was of intrahepatic or extrahepatic origin. The observed physical findings, symptoms, and laboratory results in these groups are presented in tables 1 and 2.

Symptoms and Physical Signs

As noted in table 1, the great majority of patients with jaundice of intrahepatic origin manifested prodromal symptoms of nausea, vomiting and malaise (91 per cent). These symptoms, as might be expected, were also found in a significant but smaller percentage (73 per cent) of the patients with extrahepatic jaundice. It was of interest that the patients with intrahepatic disease had chills and fever significantly more often than those with obstructive disease (63:18 per cent). Right upper quadrant pain was a common physical finding in both groups but was more frequent in the extrahepatic group. A palpable liver was noted at the time of admission in 67 per cent of the patients with intrahepatic disease in sharp contrast to the infrequency (18 per cent) with which this physical finding was observed in the obstructive group. Although the spleen was palpable in only 8 per cent of the intrahepatic group, it was never found to be palpably enlarged in the extrahepatic group.

These observations indicate that in many instances, an accurate presumptive diagnosis can be reached purely on the basis of the history and physical signs. There is, however, a minority group in which the findings will either be inadequate or confusing. In this group, further information can be derived from the available tests of liver function.

Blood Chemistries

The liver chemistries evaluated in this study were the cephalin flocculation, thymol turbidity, total and direct bilirubin, and alkaline phosphatase.

Patients with intrahepatic disease routinely showed an initial elevation of the cephalin floc-

culation and thymol turbidity; the levels attained were usually indicative of severe hepatocellular dysfunction. These tests were less frequently (36 per cent) elevated on initial examination and did not reveal as significant a degree of abnormality in the patients with extrahepatic obstruction. No increase in the degree of hepatic dysfunction was noted in the latter group during the period of observation before operation.

It is particularly interesting to note that in this early phase of the disease the majority (79 per cent) of patients with jaundice of intrahepatic origin had alkaline phosphatase values between 5 and 15 Bodansky units, whereas only 46 per cent of the patients with obstructive jaundice had elevations in this range. However, only 3 of the 24 patients with intrahepatic jaundice (12.5 per cent) had initial levels greater than 15 units; in the obstructive group a significantly greater number (36 per cent) revealed an elevation of this degree. Furthermore, whereas 75 per cent of the patients in the intrahepatic group had total bilirubin values greater than 4 mg. per cent and levels of direct reacting bilirubin greater than 3 mg. per cent, less than half of the patients in the obstructive group had comparable values.

TABLE 1

Presenting symptoms and physical signs

Symptoms	Intrahepatic*		Extrahepatic†	
	No.	%	No.	%
Nausea, vomiting malaise	22	91	8	73
Fever, chills	15	63	2	18
Palpable liver	16	67	2	18
Palpable spleen	2	8	0	0
Right upper quadrant pain	15	63	10	91

* 24 patients.
† 11 patients.

DISCUSSION

The presenting symptoms and physical signs found in the patients with intrahepatic disease in this series were classical and usually suggested the cause of jaundice. The high incidence of fever and chills in the intrahepatic group is especially striking and is contrasted to a significantly lower incidence of these symptoms in the extrahepatic group. The latter observation, in contradistinction to other reports,[3] implies that ascending cholangitis is rarely present in the extrahepatic group during this early phase of the disease. A palpable liver and spleen at the time of the initial examination strongly suggest intrahepatic disease. If, in addition, chills and fever are observed, the diagnosis of intrahepatic disease is almost certain. It is significant that in the patients in this series, a history of dark urine and acholic stools was not particularly helpful in determining the cause of jaundice. Examination of the urine for bile and urobilinogen content, on the other hand, was frequently helpful.[1, 5]

The standard laboratory chemical tests of liver function are of unquestioned value in the differentiation of intrahepatic and extrahepatic disease but can be accurately interpreted only if they are assessed in relation to the duration of disease, the history and the physical findings. In this study, evidence of parenchymal liver disease was revealed even in the earliest stages of jaundice by the thymol turbidity and cephalin-

TABLE 2

Blood chemistries

	Intrahepatic				Extrahepatic			
	Admission		2 weeks		Admission		2 weeks	
	No.	%	No.	%	No.	%	No.	%
Cephalin flocculation > 1.0	21	88	21	88	4	36	1	1
Thymol turbidity > 5.0	21	88	21	88	4	36	1	1
Alkaline phosphatase 5 to 15 Bodansky units	19	79	19	79	5	46	3	27
Alkaline phosphatase > 15 Bodansky units	3	12.5	2	8	4	36	0	0
Bilirubin total > 4.0	18	75	7	29	5	46	0	0
Bilirubin direct > 3.0	17	71	7	29	5	46	0	0

cholesterol flocculation tests. As would be anticipated, the patients who demonstrated a significant degree of hepatocellular dysfunction as measured by these tests were usually proved to have jaundice of intrahepatic origin, although slightly more than a third of the obstructive group revealed some deviation from normal. The degree of abnormality, however, was invariably greater in the intrahepatic group. One of the most significant findings in this study is the observation that, during the early phase of jaundice, neither the degree of bilirubinemia nor the proportion of direct reacting bilirubin is a reliable index of extrahepatic obstruction. The alkaline phosphatase test was of little value in differentiating between the two types of jaundice unless an elevation greater than 15 Bodansky units was present, in which case extrahepatic biliary disease was usually present.

In the patients with parenchymal disease, the initial laboratory studies were invariably abnormal and for the most part remained unchanged over the 2-week period of consideration. The tests of hepatocellular function remained consistently elevated as did the less severe degrees of alkaline phosphatase abnormality. Of 3 patients in this group who initially showed an alkaline phosphatase value greater than 15 Bodansky units 1 was found to have a value of less than 15 after 2 weeks. The only striking change among this group was a marked decrease in the level of both total and direct reacting bilirubin. In the extrahepatic group, none of the abnormal laboratory tests changed significantly during the period of observation before operation.

Two patients, in whom initial studies were equivocal, underwent laparotomy. The symptoms, physical findings and laboratory examinations in these patients were generally indicative of intrahepatic disease, but a markedly elevated alkaline phosphatase suggested the possibility of obstruction. At operation, however, no obstruction in the extrahepatic biliary system was found in either case. Liver biopsy taken at operation revealed hepatitis in both.

Although certain of these results seem paradoxic, they are consistent within the patients in this study. It would appear that these tests may be considered as reliable evidence in the differentiation of jaundice of intrahepatic and extrahepatic origin even in the very early stages of the disease. The correct interpretation of these tests during this period, however, requires recognition of the peculiarities noted above. Reliance upon a single test of function is dangerous and may lead to distressing results as illustrated by the 2 patients with hepatitis in whom operation was performed on the basis of an elevated alkaline phosphatase.

It is apparent that each of these points may be of value in the differentiation of intrahepatic and extrahepatic disease but that in a given patient, any single finding may be misleading. If the sum of these factors is considered, however, it should be possible to determine the nature of the disease in the great majority of patients even in the earliest stages of clinical jaundice.

A 5-year follow-up of each patient did not result in reclassification of the diagnosis of intrahepatic or extrahepatic type jaundice.

SUMMARY

1. Jaundice of acute onset was studied early in the course of the disease in 35 patients; 24 of these patients proved to have jaundice of intrahepatic origin whereas 11 patients were shown to have extrahepatic obstruction.

2. A palpable liver and spleen at the time of the initial physical examination strongly suggests intrahepatic disease as the cause of jaundice as does a history of fever and chills.

3. Patients who demonstrated a significant degree of hepatocellular dysfunction in the acute phase were usually proven to have jaundice of intrahepatic origin.

4. During the early phase of jaundice, bilirubinemia was not found to be a reliable index of extrahepatic obstruction.

5. The alkaline phosphatase was not of assistance in differentiating between obstructive and parenchymal disease unless the value was greater than 15 Bodansky units.

6. In the early phase of jaundice of acute onset, the liver function tests may be misleading unless they are interpreted with respect to the peculiarities noted.

7. Excessive reliance on a single chemical test for the differentiation between jaundice of intra-

hepatic and extrahepatic origin is most unwise, since considerable variation is noted in all tests of function examined in this study. The sum of the evidence was sufficient to indicate the correct diagnosis in every instance, even in the earliest stages of clinical jaundice.

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REFERENCES

1. Child, C. G., III, and Payne, M. A.: Hepatic physiology and the surgical patient. S. Clin. North America, *32:* 599, 1952.
2. Ellis, D. S.: Jaundice, its differential diagnosis. M. Clin. North America, *41:* 1345, 1957.
3. Lien, R. C., and Maddock, W. E.: Jaundice, differential clinical and laboratory diagnosis. S. Clin. North America, *36:* 131, 1956.
4. Trimble, I. R.: The differential diagnosis of jaundice with special reference to its surgical treatment. Am. Surgeon, *25:* 201, 1959.
5. White, F. W.: A study of errors in the diagnosis of jaundice. New England J. Med., *299:* 997, 1943.

THE PRESENT STATUS OF SURGICAL TREATMENT OF PATHOLOGIC AFFECTIONS OF THE THYROID GLAND

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Over the past 30 to 40 years, a large number of innovations have been instituted in the treatment of the various pathologic conditions occurring in the thyroid gland. As a result, the literature published upon this subject has been highly controversial and caused a great deal of confusion in the minds of both internists and surgeons alike. It is the purpose of this report to discuss surgical diseases of the thyroid gland, with particular emphasis on carcinoma, and the rationale of treatment.

HYPERTHYROIDISM

In no disease, perhaps, is the treatment less stereotyped or uniform than in cases of severe hyperthyroidism or exophthalmic goiter. Each case is a law unto itself and should be studied in every detail from the clinical, laboratory, and in a large number, from the sociologic standpoint. Each patient presents an individual problem modified by many subsidiary facts, and the type of treatment to be instituted must be elastic and adaptable to every variety of case. It is now conceded that the most efficacious method of treating hyperthyroidism is one which combines both medical and surgical measures. Alone, either will be found inadequate for the great majority of cases. They call for the constant and closest cooperation between the internist and the surgeon from the very beginning of the treatment, so the clinical course will be absolutely familiar to both. Unfortunately, although such close cooperation between the internist and surgeon prevailed during the era when iodine in the form of Lugol's solution constituted the recognized preoperative preparation, since the advent of the use of propylthiouracil and radioactive iodine, the management of the treatment of hyperthyroidism has been taken over almost exclusively by the internist. Not only does the surgeon fail to come in contact with the patient before medicinal therapy has been begun, but also only sees the patient in whom medicinal therapy has been unsuccessful or in whom complications due to the antithyroid drugs have ensued. The surgeon, therefore, has no knowledge of the patient's previous condition. Furthermore, because the patient has become euthyroid from a laboratory standpoint does not mean the hyperthyroidal state has been cured. In most cases, hyperthyroidism cannot be treated definitively by medical means, so it is the responsibility of the internist to bring about a euthyroid state before the final phase of treatment is undertaken, whether it is thyroidectomy or in some exceptional cases, radioactive iodine.

Clinical experience indicates that there are two distinct types of hyperthyroidism which vary widely in their clinical manifestations and responsiveness to treatment. Adenomatous goiter differs from Graves' disease in many respects, not only clinically, but in response to treatment with antithyroid therapy. Both Graves' disease and adenomatous goiter, or nodular goiter, may present all the laboratory data and clinical manifestations of hyperthyroidism, or on the other hand, show a minimum of clinical signs with normal laboratory data. Response to antithyroid medicinal therapy in adenomatous goiter is even less predictable than in Graves' disease. In the latter, a permanent remission after discontinuance of the drug will occur in less than half of the patients, even though they were under the continuous administration of the drug for 2 and often 3 years. More than half of the cases will suffer exacerbation of the signs and symptoms of the disease upon discontinuance of the antithyroid drugs. In the adenomatous goiter with hyperthyroidism, the failure to maintain a permanent remission is well over 75 per cent. It is to be noted that in the medically treated patients that are not in a permanent remission, the disease process has continued and unknown damage to the patient may have been incurred.

Even in the event of a euthyroid state which

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can only be maintained by the continuous use of an antithyroid drug such as propylthiouracil, the gland is in a constant state of hypertrophy and hyperplasia. It is well known that the block in the production of thyroxine occurs in the epithelial cells of the gland, in spite of the fact that inorganic iodine is taken up by the gland. The conversion into organic iodine, however, does not occur, and this results in the formation of various partially iodinated thyronines and related analogues, as well as other compounds as yet unidentified. No one, at present, knows the harmful physiologic effects that such compounds may produce, but clinically, in addition to the persistence of a goiter or even a gradual increase in its size, there is a continuous intoxication that has various side effects. One of the most distressing is permanent paralysis of one or more of the extraocular muscles, particularly the superior rectus, resulting in a vertical diplopia. (We have observed this in 2 cases in which propylthiouracil was given over a period of 2 years.) Biopsies before and after an extended period of treatment with any of the antithyroid drugs have shown that the gland never reverts to a normal histologic status. In some patients in whom the enlargement of the thyroid gland has attained such enormous proportions under the continuous use of propylthiouracil, the individuals have been unable to assume a recumbent posture because of dyspnea. (One of these patients was pregnant and when the baby was born, the latter also had a marked enlargement of the thyroid which nearly proved fatal.) In such patients, despite operation and the administration of Lugol's solution, for 3 weeks preoperatively, involution does not take place. The operations are very difficult because of the vascularity and friability of the gland; thus, the danger of injuries to the recurrent laryngeal nerves and the parathyroid glands are greatly increased.

The available methods of treatment of patients with hyperthyroidism are, of course, directed at alleviating overactivity of the thyroid gland, whether it be an instance of Graves' disease or adenomatous goiter. The methods that may be used and which have proved most successful in the long run have been thyroidectomy and, for certain exceptional cases, radioactive iodine. Before using either one of the above methods, the patient should be euthyroid or approximately so. However, with the advent of antithyroid drugs, the preoperative preparation of patients with Lugol's solution has been all but forgotten. It is not necessary in the average, moderately severe case of Graves' disease to have the patient absolutely euthyroid. A great deal of time and expense can be saved for many patients by a 2- to 3-week hospitalization on Lugol's solution, 10 drops twice a day, followed by thyroidectomy. In the more severe cases of Graves' disease, propylthouracil should be used and the patient made euthyroid before operation or radioactive iodine. In some mild cases of Graves' disease, with small thyroid glands, a permanent remission may be obtained by the use of one of the antithyroid drugs alone, but these are the exceptions that prove the rule. In older people, 50 to 80 years of age, with Graves' disease, radioactive iodine may be used with success and without fear of the development of a malignant change in the scarred thyroid years later, as might be the case in younger patients. Both iodine and radioactive iodine are relatively inefficacious in treating adenomatous goiter with hyperthyroidism. Even with antithyroid drugs, the return to a euthyroid state requires much more time in the adenomatous goiter than in Graves' disease. The ideal treatment for adenomatous goiter is thyroidectomy after proper preparation. The recurrence rate after thyroidectomy for Graves' disease is less than 1 per cent. In adenomatous goiter with hyperthyroidism, recurrence or myxedema does not occur after subtotal thyroidectomy.

In reviewing 1784 thyroidectomies performed in The Johns Hopkins Hospital in the past 12 years, Asper[1] found transient hypoparathyroidism in about 9 per cent, with unilateral recurrent laryngeal palsy in 5 per cent. Postoperative myxedema occurred in 4 patients. It would, therefore, seem apparent that the results of surgical ablation of the thyroid gland for hyperthyroidism are at the present time better than those obtained by prolonged medicinal therapy, and safer than the use of radioactive iodine.

Continuous antithyroid drug therapy is invaluable in the treatment of hyperthyroidism complicated by conditions in which the use of other methods of treatment are contraindicated or hazardous. The most notable example of this sort of situation is in the first 6 months of pregnancy, but not in the last 3 months when the

fetal thyroid begins to function. One of the most distressing complications that occurs after antithyroid drug therapy, radioactive iodine (I^{131}) and surgery, is progressive exophthalmos. These patients normally complain of burning, excessive lacrymation and protrusion of the eye bulbs. The signs and symptoms of hyperthyroidism are minimal and the gland is generally small. Surgical removal of just a sufficient amount of thyroid tissue to control the minimal overactivity of the gland is desirable. If too much of the gland is thrown out of function, the exophthalmos becomes continuously worse, and they suffer great discomfort and incapacitation. Because of the lack of certainty in the dosage and the extent to which the thyroid in different individuals will take up the radioactive iodine, this method of ablation of the thyroid gland is not so satisfactory as thyroidectomy when one can see the size of the thyroid and judge more accurately the amount that should be removed. The "guess dose" of radioactive iodine may cause more of the gland to be ablated than was intended or desirable.

The indications for surgical removal of 90 per cent of the thyroid gland in thyrotoxicosis may be listed as follows:

1. In those patients with diffuse goiter who fail to respond favorably to the antithyroid drugs or in whom a permanent remission cannot be maintained.

2. In hyperfunctioning adenomatous goiter, whether there is present single or multiple nodules.

3. In an as yet unknown percentage of patients whose thyroid glands continue to enlarge during the prolonged use of the antithyroid drugs. Such enlargements continue to grow so much that they cause dyspnea and dysphagia even when the patient remains in the sitting position.

4. In severe thyrotoxicosis associated with pregnancy. Radioactive iodine will be retained in the fetal thyroid with possible latent genetic effects.

5. In those patients with moderate or low grade hyperthyroidism who can be properly prepared with Lugol's solution.

The uniformity of opinion as to whether radioiodine or surgery should be the preferred type of definitive therapy in any given case of hyperthyroidism would be almost impossible to obtain. Some individuals are still of the opinion that all cases of thyrotoxicosis should be treated by surgical means. This attitude, it seems to me, is unfortunate because of the fact that there are individuals who, under certain circumstances, should be treated by medicinal or isotope therapy. There are also individuals who go to the opposite extreme and think all cases of thyrotoxicosis should be treated with I^{131}. This attitude is also a dangerous and unfortunate one. It is to be noted that irradiation therapy of any type in children has in a relatively high percentage of cases been followed by the development of carcinoma of the thyroid, this therapy having been used for lesions of the upper respiratory tract or thymus. It would seem, therefore, illogical in the extreme to administer radioactive compounds to children suffering with thyrotoxicosis. It is also to be noted that in the treatment of hyperthyroidism associated with pregnancy, the use of I^{131} may have a genetic effect because of the fact that the fetal thyroid concentrates iodine, and it has been demonstrated also in the milk of lactating mothers.

It is my opinion that I^{131} should not be used in persons with either a single or multiple nodular goiter because of the high incidence of carcinoma in clinically solitary nodules, and although the occurrence in multinodular goiter is not as great, it is still a factor to be taken into consideration.

It is probably advisable to administer I^{131} in cases of: (1) recurrent or persistent hyperthyroidism after thyroidectomy; (2) hyperthyroidism with severe cardiovascular disease or some other concurrent disease; (3) in the event a patient refuses to accept surgical or other therapy. In patients under 40 years of age, it would seem inadvisable to use this type of therapy because of the possibility of delayed carcinogenic activity of this isotope. It will require many years to evaluate fully any possible long range harmful effects of beta radiation on the thyroid or other tissue. Therefore, I feel that patients under 40 years of age, with uncomplicated hyperthyroidism, should be treated by surgery. In skilled hands the risk of surgery in this group is minimal. The mortality should be less than 0.5 per cent and the complications less than 1 per cent. Thus, there is very little mortality, and the results are excellent. In the average run-of-the-mill case of hyperthyroidism, preoperative preparation with Lugol's solution for 2 to 3 weeks is generally

sufficient as preoperative medical preparation. In the older group, the 7th and 8th decades, the use of I^{131} certainly should be given serious consideration.

The primary carcinomas of the thyroid are a heterogenous group of lesions of markedly different histologic structure and biologic behavior. The less anaplastic lesions have proved particularly troublesome. Their benign histologic appearance or their apparently benign course is so at variance with the current conceptions regarding carcinoma that the lesions are usually considered benign. Thus, the only primary carcinomas originally recognized were the more anaplastic lesions, the treatment of which was then and is now most unsatisfactory.

The resulting pessimism regarding carcinoma of the thyroid, because of this fact, is at present quite unfounded. Among current cases, less than 20 per cent of lesions are of the anaplastic type. As with many other malignant lesions, until better diagnostic or therapeutic methods become available, there is little hope that ultimate results after treatment of lesions of the anaplastic can be materially improved. This is decidedly not the case with all other types of carcinoma of the thyroid. Therapeutic methods currently available are quite adequate, providing only that the lesion is not inoperable. Furthermore, there is every reason to believe that the proportion of lesions found inoperable at present can be materially reduced, primarily through the routine removal of nodular goiters.

A broader understanding of carcinoma of the thyroid would unquestionably also contribute to better ultimate results. The apparent marked differences of opinion regarding several aspects of the problem have done much to perpetuate some of the confusion of the past. Such differences are far more apparent than real. There are at least 3 widely used pathologic classifications, which superficially seem to differ from each other markedly. However, they are, in fact, quite similar and need cause little confusion. The different pathologic criteria employed by different pathologists result in rather uniform diagnoses. In spite of the difficulties of microscopic diagnosis, particularly of malignant adenomas, a lesion considered malignant at one institution is practically always considered malignant at another. The indications for resection of regional lymph nodes and the extent of the operative procedure have been relatively standardized, in spite of the use of different terms to describe the operative procedures. There is perhaps some true difference of opinion regarding external irradiation, but practically the differences are not important. For clinical purposes, current knowledge regarding carcinoma of the thyroid is reasonably comprehensive, and the confusion that has surrounded the subject for years has been largely dispelled.

It is of the greatest importance that the surgeon, who takes upon himself the responsibility of the care of a patient with one of the various types of carcinoma of the thyroid, should have a clear-cut philosophy and plan of operative procedure suited to the type of malignant tumor encountered. Unfortunately, particularly in the papillary type of adenocarcinoma, a frozen section of the tissue removed at the time of operation may be confusing; but these instances are the exceptions which prove the rule. The surgeon should be guided by the pathologist as far as possible in order to avoid not only performing an unnecessary radical operation but also an inadequate one. The tragic examples that are so frequently seen following such operations are generally due mainly to a lack of understanding on the part of the operator of the pathogenesis and progression of certain thyroid malignancies and thus performing an inadequate dissection of cervical lymph glands and the thyroid itself. It is not always possible even under the most favorable circumstances to be absolutely certain of the exact histologic characteristics of the tumor in question, because some are pleomorphic. In such an event it is better to err on the side of a thorough removal of the thyroid and its associated lymph glands than otherwise. Excepting the anaplastic carcinomas, practically all types of malignant epithelial tumors of the thyroid can be cured if operated upon before the tumor has spread beyond the confines of the thyroid gland.

All symptoms and signs of carcinoma of the thyroid, except for the nodule in the thyroid, develop relatively late in the course of the disease. By the time that the diagnosis is suspected or can be made with some certainty on clinical examination, the lesion either has metastasized or has spread beyond the capsule of the thyroid. As with other malignant lesions, but particularly so for lesions of the thyroid, the

interval between development and spread is the interval during which treatment has the best chance of succeeding. In the majority of carcinomas of the thyroid, this interval before spread is prolonged. Any real hope of materially improving results, using present known methods of treatment, lies in removing the malignant nodule before it has spread, or for practical purposes, before symptoms suggestive of malignant change have made their appearance. This implies that nontoxic nodular goiters should be removed more or less routinely.

Although the true incidence of carcinoma in nodular goiter is unknown, there is considerable information concerning the incidence of carcinoma in nodular goiters that have been removed surgically. This incidence in surgical material as reported in recent years, with few exceptions, varies from 5 to 33 per cent.

A most important point to be stressed is that the solitary thyroid nodule carries a much greater incidence of malignancy than does the multinodular lesion. Lahey and Ficarra[4] and Cole and his associates[2] emphasize this. Cole reported 24 per cent of solitary nontoxic nodules were malignant, but only 11 per cent of the multinodular nontoxic glands as malignant. Thus 1 in 4 of the solitary nontoxic goiters was cancerous. The size of the nodule is unimportant since carcinoma has been found in adenomas only a few millimeters in diameter. The Lahey Clinic in reviewing all patients with thyroid cancer treated during 1951 and 1952 found 52 cases of malignancy in a group of 156 with discrete nontoxic nodules, an incidence of 33.3 per cent. Therefore 1 out of 3 solitary nontoxic nodules was cancer. If all types of nontoxic nodular goiter are included, multiple as well as single, the occurrence of carcinoma was 10.2 per cent. The Hospital of the University of Pennsylvania reported that of 1523 surgically treated nodular thyroid lesions between 1945 and 1952, 174, or 11.4 per cent, were cancer.

My personal series of cases of diseases of the thyroid gland upon whom I have operated, made histologic studies of the operative specimens removed, and followed up the patients after discharge from the hospital, now totals 2489 patients. This number includes all types of diseases of the thyroid gland; 87, or 3.4 per cent, in this group proved to be malignant. Of this total of 2489 patients 1029 of them were found to have nodular goiters of which 87, or 8.5 per cent, proved to be carcinoma; 686 of the 1029 were solitary nodules in which 17 per cent were considered to be malignant on pathologic examination.

Of 87 patients followed we were unable to trace 30, but received information on 57, in which 32, or 56.2 per cent, were living and 25, or 43.8 per cent, were dead. In the group that had died from 1 to 4 years postoperatively, the malignant growth had spread beyond the confines of the original nodule. In each of these patients malignancy was suspected clinically before operation. In contrast to this group, the patients that have survived, *i.e.*, 56.2 per cent, for 5 years or more were thought to have clinically benign nodules. In this group the pathologic diagnosis of malignancy was made within the confines of the nodule. It would therefore seem reasonable to assume that if solitary nodules are removed from the thyroid gland by surgical excision while they are yet clinically benign, even though a pathologic diagnosis of malignant change confined to the nodule is reported, the patient has an excellent chance of permanent cure. Conversely, if the malignant change has spread beyond the confines of the nodule, the prognosis is markedly worsened. This is particularly true of all varieties of carcinoma, even the well differentiated slow-growing types. In the latter types, *i.e.*, the so-called malignant adenoma or adenocarcinoma and also the papillary group, on account of their slow growth some years may pass before a recurrence due to a previous spread beyond the confines of the nodule may manifest itself.

In a current but as yet incomplete study of all cases of carcinoma of the thyroid operated upon in The Johns Hopkins Hospital from 1925 to 1956, there were 170 instances. The majority of these cases were included in my personal series cited above, but there were a few additional patients operated upon by the various members of the visiting or house staff. Dr. James Jude, a member of the resident surgical staff, permitted me to quote these figures from a detailed pathologic study. The sex distribution of this group corresponded to other reports in the literature in showing a predominance of females, 126 to 44 males. The age distribution was also typical (fig. 1) demonstrating a high incidence of the well differentiated and therefore curable types of

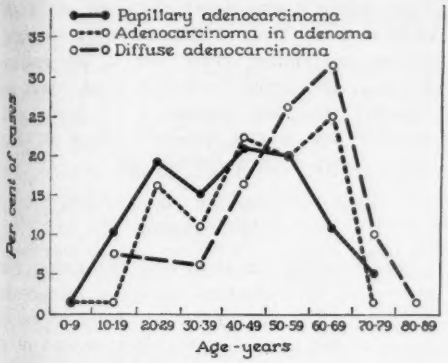

FIG. 1. Age distribution of different types of carcinoma of the thyroid.

carcinoma in the younger age groups, the 2nd, 3rd and 4th decades, with a preponderance of the more anaplastic or undifferentiated tumors, the incurable ones, in the 5th and 6th decade. By far the greater number of malignant tumors of the thyroid glands in this series, 107, or 63 per cent of the 170 total, were the well differentiated slow-growing type that could be permanently cured if adequate early removal was employed. The primary clinical examination revealed obvious carcinoma in 34 patients, or 20 per cent; a negative thyroid examination in 22 cases, or 13 per cent; palpable lymph nodes in 58 patients, or 35 per cent; a single palpable nodule in 63, or 37 per cent, of those later to be found to have carcinoma. It is somewhat surprising that the reported rates are so consistent, depending as they must to a large extent on the proportion of nodular goiters in which resection is advised. The findings of the Mayo Clinic, as reported by Pemburton and Black,[5] which may be taken as representative, will be quoted since large numbers of cases are involved and since recent data are available.

During the decade from 1939 through 1947, the incidence of carcinoma in resected nodular goiters was 4.8 per cent. The term "nodular goiter" is used here to designate all goiters, including clinically evident carcinomas, that were nodular on clinical examination. The figure is somewhat meaningless as a measure of the incidence of unsuspected carcinoma in nodular goiter, since clinical acumen extends far beyond the mere palpation of nodules. The incidence of carcinoma not evident as such on clinical examination varies with the presence or absence of toxicity, with sex and with age.

Adenomatous goiter with hyperthyroidism and carcinoma. During the decade covered in the review, thyroidectomy was carried out because of adenomatous goiter without hyperthyroidism in 3247 cases. A carcinoma was found in the resected tissue in 244 cases (7.5 per cent). This incidence, while in keeping with that reported by others, is misleading in that clinical impression as to the possibility of carcinoma was purposely not considered. In 126 of the 244 cases, there was some indication in the record that carcinoma was suspected preoperatively. In 3121 of the 3247 records, there was no indication of such suspicion. Yet in the group there were 118 carcinomas, all of which were recognized first either when the thyroid was resected or on pathologic examination. They believe that this incidence of 3.8 per cent is a fair estimate of the incidence of clinically unrecognizable carcinoma in cases of adenomatous goiter without hyperthyroidism.

The chance of finding carcinoma in solitary nodular goiter is undoubtedly greater than in a multiple nodular goiter. As Cope[3] and his colleagues have pointed out, carcinoma begins as a localized change in the thyroid. If only goiters in which the pathologic changes are limited to one region are considered, the proportion of carcinomas will be higher than if, in addition, thyroids in which the changes are generalized are included. They found the incidence of carcinoma in clinically solitary nodule to be approximately twice as great as in all nodular goiters without hyperthyroidism. This finding is in accord with our clinical impression.

Carcinoma is far less likely in the presence of hyperthyroidism than in its absence. Among cases in which the clinical diagnosis was adenomatous goiter with hyperthyroidism, the incidence of carcinoma was slightly less than 1 per cent, whereas among cases of exophthalmic goiter the incidence was less than 0.5 per cent. The possible presence of carcinoma in association with toxic goiter is of minor practical importance, since toxic nodular goiters are usually resected and tissue is thus available for microscopic examination. The malignant lesions found in association with exophthalmic goiter are practically always minute papillary lesions, probably of little clinical significance. If some form of treat-

ment other than resection is chosen for toxic nodular goiter, the possibility of unsuspected carcinoma, however, should be considered.

Age. Although carcinoma of the thyroid has the usual age distribution of other carcinomas (fig. 1), it is not particularly uncommon in children. Two to three per cent of all thyroid carcinomas occur in children less than 14 years of age, whereas approximately one-third of all papillary lesions occur in children and young adults. The proportion of cases of nodular goiter in which a malignant lesion is found is greater the younger the patient. In children 14 years of age or less, fully one-third of nodular goiters are malignant. Although the proportion of cases in which the lesion is malignant declines rapidly after puberty, the incidence in those less than 30 or 35 years of age is far greater than in older patients. The reason probably has to do with the fact that benign nodular goiter is unusual in young persons and becomes progressively commoner with increasing age. Consequently, the proportion of nodular goiters that are malignant declines from an extreme high in childhood to a relatively low figure in old age. The neglect of a nodule in the thyroid of a child until it is clinically diagnosable as carcinoma, and hence frequently inoperable, is particularly unfortunate, since treatment is notably successful before this stage has been reached.

Dr. Samuel Asper, a member of the medical staff in charge of the thyroid clinic at The Johns Hopkins Hospital, informed me that of 17 patients under 20 years of age with carcinoma of the thyroid, 9 had received some form of x-ray radiation therapy in infancy or childhood. Four received radiation to the thymus, one to laryngeal papilloma, one external radiation to the tonsils, two radiation to the nasopharynx and one radiation to the base of the tongue. In each instance it seems likely to me that the thyroid region was also in the portal. Thus, there is an apparent relationship between x-ray radiation given in infancy or childhood and the later development of thyroid cancer. Duffy and Fitzgerald at the Memorial Hospital in New York had 10 of their 28 juvenile patients with thyroid cancer with such history of radiation. Clark in Chicago had 15 patients, each of whom had a history of radiation. The best control study comes from the group in Rochester, New York, where it was shown that, out of 14,000 children given x-ray radiation to an enlarged thymus in infancy, there was a far greater incidence of thyroid carcinoma than could be expected from the population at large and certainly far greater incidence than in the control group of untreated siblings.

SIGNS AND SYMPTOMS OF CARCINOMA OF THE THYROID

Before listing the signs and symptoms, the genesis of such changes might be considered profitably. The first clinical evidence of carcinoma of the thyroid is the development of a nodule within the gland. Rarely, metastatic deposits in cervical lymph nodes, bones or lungs may appear before the nodule in the thyroid is evident clinically. However, it is most unusual not to be able to find some abnormality of the thyroid by the time metastatic growths have become clinically evident. In the case of encapsulated carcinomas, particularly of malignant lesions that apparently develop in adenomas, findings suggesting that the lesion is malignant begin to appear when the carcinoma infiltrates the capsule of the lesion. After this has occurred, the form of the nodule tends to become irregular, and the mass becomes less movable with the parenchyma of the lobe. Similarly, the relative fixation and irregular shape of the nonencapsulated lesions ultimately become evident on clinical examination if the lesion is sufficiently large. The characteristics of the nodule are more readily appreciated if the lesion develops near the anterolateral capsule of the lobe. They are far less evident in the case of nodules situated deeply within the lobe or near the posterior capsule. Ultimately, the infiltrating malignant tissue extends through the capsule of the thyroid to involve surrounding structures. At this stage, for the first time, excluding from consideration metastatic growths and their manifestations, the correct diagnosis becomes more or less obvious clinically. Unfortunately, by this time, involvement of surrounding structures often precludes the possibility of complete removal. At the present time fully one-third of all carcinomas of the thyroid prove inoperable, in the sense that not all of the malignant issue can be resected by the time definitive treatment is first attempted. This proportion of inoperable cases is far higher than that of the

breast or colon and closely approaches that of the stomach.

A history of the relatively sudden appearance of a nodule within the thyroid or of the sudden development of a goiter is of course suggestive of carcinoma. Similarly, the history of a progressive increase in size of a nodule or of the gland has much the same significance. Such changes in the thyroid are often associated with a sense of pressure or with some tenderness. If such symptoms are produced by the carcinoma, the lesion is likely to be rapidly growing and anaplastic, or if less anaplastic, it has transgressed the capsule of the gland. In either case, the symptoms are late and of advanced lesions. A nodule said to have appeared recently usually, in fact, has been present for some time but has only recently been discovered by the patient. Hemorrhage into an adenoma and certain types of thyroiditis may cause localized changes quite indistinguishable clinically from those resulting from carcinoma. Perhaps the best clue to the presence of a reasonably early (in the sense that the lesion is resectable) carcinoma, apart from the mere presence of a nodule, is the character of the nodule. The important point here is that the nodule differs on palpation from other nodules in the gland or from the surrounding thyroid tissue. The irregularity of carcinomatous nodules and their relative fixation within the gland have been discussed. A carcinomatous nodule, although traditionally firmer than a benign nodule, may not be particularly hard and may, in fact, be definitely softer than many benign nodules. In this connection, calcification in a nodule does not exclude the possibility of a malignant lesion, since calcification in a malignant nodule, particularly in papillary lesions, is fairly common. In cases in which the involvement of the thyroid is more extensive, the consistency is as a rule far firmer than that of benign goiters. This, coupled with surface irregularities, or an outgrowth beyond the general profile of the gland, is most suggestive of cancer. Riedel's struma (woody or fibrous thyroiditis) is associated with identical findings. The clinical diagnosis in cases of Riedel's thyroiditis should invariably be carcinoma, since the gross findings, both clinically and at operation, are identical in the two conditions. With advanced carcinoma, the thyroid, or that part of the gland involved, becomes fixed to surrounding structures. Although lesions of this extent are almost invariably inoperable, the fixation occasionally is due to the mere wedging of a large goiter in the superior strait of the chest.

Malignant invasion of the posterior or posteromedial parts of the capsule may be undetected on examination; deeply situated lesions may in fact be undiagnosable until after such invasion has occurred. The clue to the presence of the lesion is provided by carcinomatous involvement of the recurrent laryngeal nerve, which leads to fixation of the corresponding vocal cord and to hoarseness. Fixation of a vocal cord because of pressure of a benign thyroid nodule may also result from mediastinal tumors or from aneurysms of the great vessels, and occasionally it is observed in cases of mitral stenosis. In the absence of such lesions, the finding is presumptive evidence of carcinoma of the thyroid. The symptoms produced by malignant invasion of other structures are always late and usually indicate inoperability. Dysphagia is usually due to malignant infiltration of the esophagus or pharynx and not to mere pressure, while stridor usually results from distortion or compression of the trachea and only occasionally from actual infiltration. The esophagus presents little barrier to infiltration, while the trachea fascia is quite resistant. In late, or particularly in terminal, cases the trachea does become infiltrated. The intratracheal malignant tissue may bleed or obstruct the airway. Similarly, the great arteries of the mediastinum and neck resist invasion, but ultimately may be eroded with resulting hemorrhage and death.

TYPES OF MALIGNANT LESIONS

The diversity of histologic features of cancer of the thyroid and the extreme variation in biologic behavior have combined to make pathologic classification most difficult. The rather simple classification favored by us at present is probably the most familiar of the classifications currently in use, and has been found adequate for the grouping of all primary malignant tumors of the thyroid.

Papillary Adenocarcinoma

Lesions of this type account for at least 60 per cent of carcinomas of the thyroid. Among current cases, the proportion of papillary lesions is probably even greater. Malignant adenomas

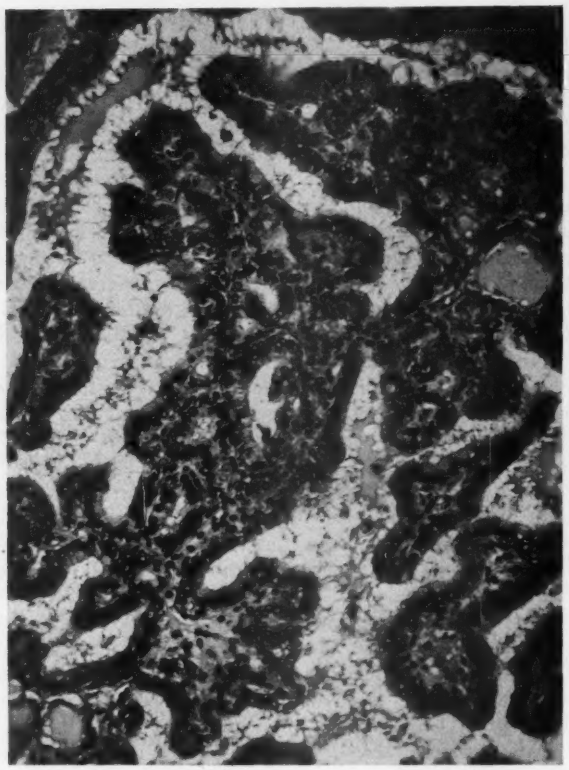

FIG. 2. Typical papillary adenocarcinoma of thyroid. × 176

formerly were seen more frequently than papillary lesions, whereas currently lesions of the latter type are 3 or 4 times as common as malignant adenomas. The explanation for the change is not entirely clear. It may well have to do with the decline in the absolute number of cases of adenomatous goiter that has occurred during recent years. Papillary adenocarcinomas vary in size from a few millimeters in diameter to huge tumors filling the lower cervical and upper mediastinal regions. They tend to be small, the usual lesion measuring not more than 2 or 3 cm. in diameter (figs. 7 and 8). They develop either from adenomatous or from extra-adenomatous tissue and are usually associated with fairly marked local fibrosis. The fibrosis is more marked in the case of extra-adenomatous lesions which, as a result, are extremely firm, than in the case of the adenomatous lesions.

Papillary adenocarcinomas are easily recognizable microscopically by their papillary structure. The entire lesion may be papilliferous (fig. 2); more usually the tumor is made up in part of solid masses of malignant cells (fig. 3). Follicle formation is not unusual in some part of the tumor. More rarely, virtually normal-appearing follicles distended with colloid may be seen. As with other carcinomas of the thyroid, the histologic pattern tends to vary from region to region; a major or minor part of the tumor, however, always has a papillary structure. In keeping with their grade of malignancy, the growth of papillary lesions is slow. In fact, a lesion of this type may be present for years without evident change and without invasion of surrounding structure. In spite of their slow progression and low grade, the nonencapsulated tumors have a marked tendency to metastasize to regional lymph nodes. Cervical or mediastinal lymph nodes are found involved in approximately half of all cases at the time of operation. Nodal involvement may be massive or limited. Curi-

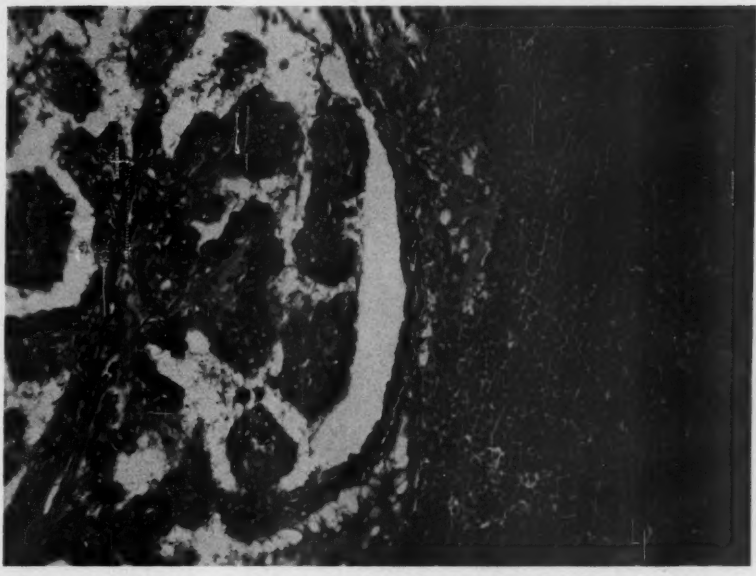

FIG. 3. Metastatic papillary carcinoma in cervical lymph gland from same case shown in figure 2. X 110.

ously, the metastatic deposits in lymph nodes tend not to invade the capsule of the nodes to involve surrounding tissues. As a result, involved lymph nodes do not become fixed and are, practically without exception, resectable. Furthermore, the metastatic deposits tend not to recur locally. This property is not shared by the primary lesion, which is slowly but definitely invasive. Ultimately, the primary lesion tends to invade the capsule of the thyroid and neighboring tissues. Distant metastatic growths are unusual even in neglected or recurrent cases. Local, unresectable extensions preclude the possibility of cure in a far greater proportion of cases than does distant spread.

Two variants of papillary adenocarcinoma have attracted special attention. These are the so-called tumors of lateral aberrant thyroid origin and the small papillary lesions occasionally found in thyroids removed for some other reason, usually because of Graves's disease. In the usual case in which the diagnosis is tumor of lateral aberrant thyroid origin, several or many of the cervical lymph nodes are enlarged, whereas the thyroid is normal on clinical examinations or contains a relatively inconspicuous nodule. The patient commonly is a young adult or a child. For some years such deposits of papillary tissue in the latter cervical region were considered to have developed from the lateral anlagen of the thyroid; hence, the name. This conception is no longer tenable. There is always a primary papillary lesion in the thyroid, and the papillary tumors in the lateral cervical regions are metastatic growths in cervical lymph nodes.

Small papillary lesions, usually a few millimeters in diameter, are occasionally found in thyroid tissue resected for some other lesion. Such lesions occur in approximately 0.4 per cent of thyroids resected because of exophthalmic goiter. The papillary tissue is usually surrounded by rather dense fibrosis, which is responsible for their having been called "sclerosing tumors of the thyroid." They differ in no way from other papillary adenocarcinomas. If the lesion is recognized before the incision is closed, total lobectomy should probably be carried out. If discovered several days after the thyroidectomy, re-exploration of the thyroid is probably inadvisable. Involvement of cervical lymph nodes is almost never observed with such tiny lesions.

Adenocarcinoma in an Adenoma (Malignant Adenoma)

The malignant adenomas were formerly the commonest of the thyroid carcinomas, from 40

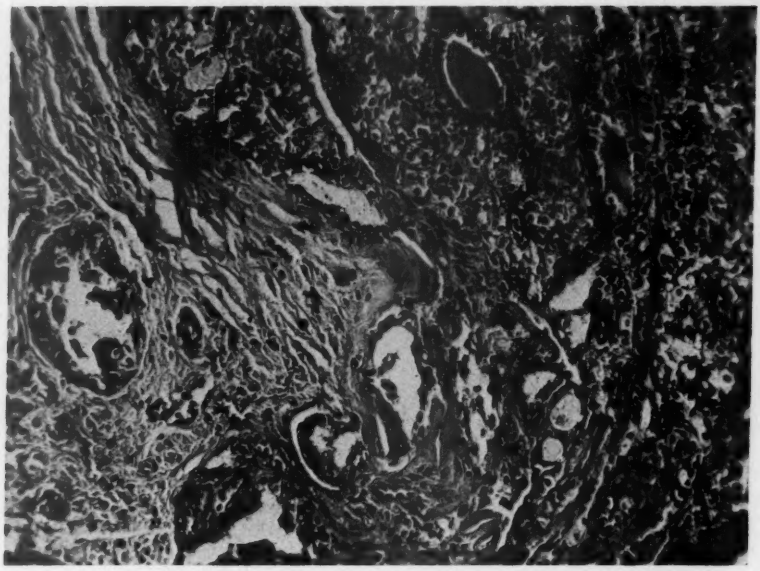

FIG. 4. Follicular carcinoma showing invasion of blood vessels. × 176.

to 60 per cent of all thyroidal carcinomas having been of this type. As previously mentioned, the relative proportion of malignant adenomas is decreasing, so that currently they are definitely less common than the papillary lesions. They are well encapsulated, although infiltration of the capsule may ultimately occur. They tend to be materially larger than papillary adenocarcinomas, varying in size as do benign adenomas. The cut surface is said to have a more or less distinctive salmon pink color in contrast to the brown or yellow-brown color of benign adenomas. Almost without exception they are of low grade malignancy.

Probably no other malignant lesion has troubled the pathologist more than malignant adenoma. Indeed, the criteria of malignancy in this type of tumor are still not settled to the satisfaction of all pathologists. The difficulty lies in the fact that the histologic structure of the malignant adenoma may be virtually indistinguishable from that of a benign adenoma. Some 30 years ago, Graham concluded that, while cytologic changes are adequate to differentiate the benign from the malignant lesion in possibly 70 per cent of cases, in 30 per cent, the distinction cannot be so made. Graham concluded that the most consistent evidence of malignancy in such lesions is vascular invasion and that such invasion, regardless of cytologic changes, is necessary to enable one to make the histologic diagnosis of malignant adenoma (fig. 4). Wegelin, in 1928, discussing the same problem, stated that the histologic structure of "metastasizing adenomas" is identical to that of benign adenomas. Other pathologists have continued to depend on cytologic differences to distinguish the benign from the malignant adenomas. With the realization that carcinomas capable of metastasizing could have a histologic appearance virtually identical with that of benign adenomas, the problem of apparently benign tissue well removed from the thyroid was resolved.

In certain classifications, Hurthle-cell carcinoma is considered as a distinct type (fig. 5). This is a well encapsulated lesion distinguished histologically by large, more or less uniform cells containing coarse eosinophilic granules (fig. 6). Its biologic behavior probably does not differ significantly from that of other malignant adenomas. Benign adenomas composed of Hurthle cells are occasionally seen, and Hurthle cells are often seen in adenomas along with other types of cells. In my opinion, there is little reason to classify Hurthle-cell carcinomas

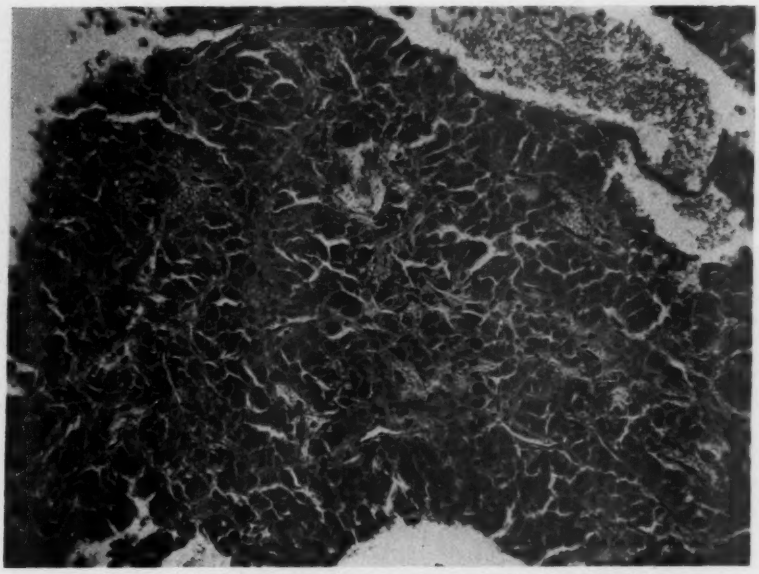

FIG. 5. Hurthle-cell carcinoma, an anaplastic type. × 176

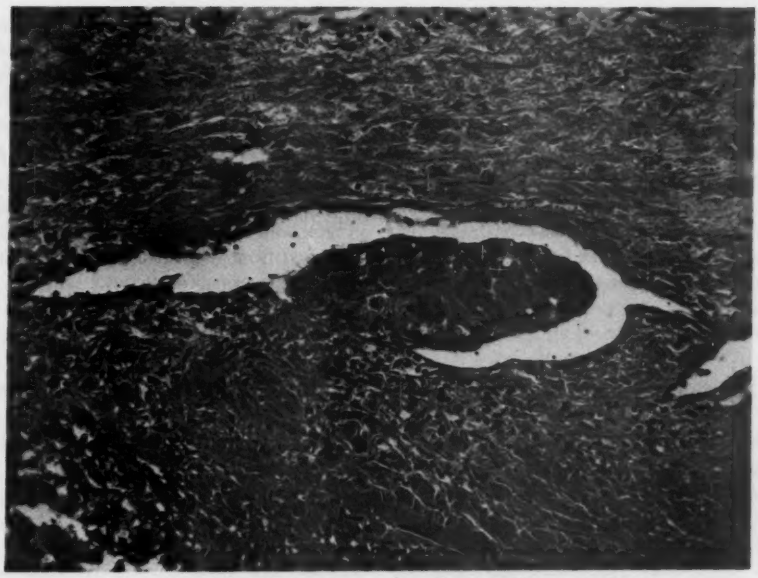

FIG. 6. Hurthle-cell carcinoma invading blood vessel. × 176

separately from other malignant adenomas, or when diffuse, from any anaplastic carcinoma.

As long as the malignant adenoma remains within its capsule, there is no possibility of lymphatic spread because adenomas have no lymphatics. After capsular invasion, the malignant cells reach the lymphatics of the parenchyma of the thyroid, and lymph-borne metastatic growths can occur. As intimated previously, the cells readily invade blood vessels within the

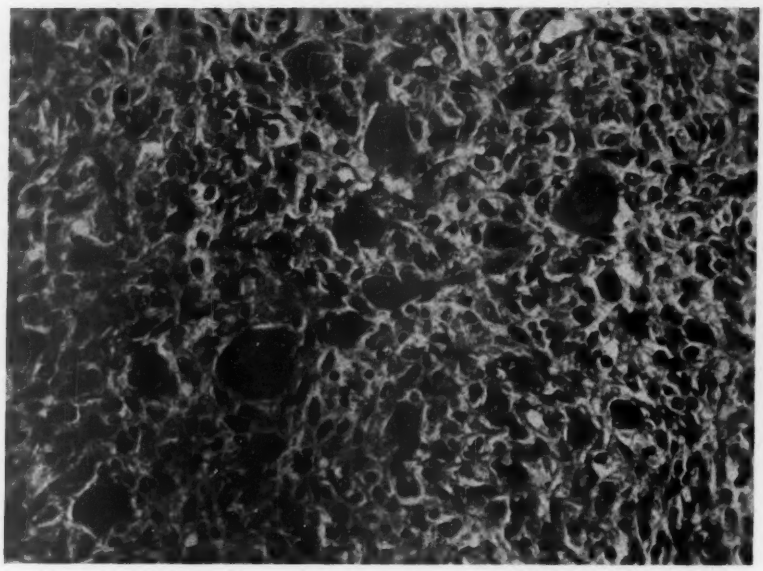

FIG. 7. Giant-cell carcinoma, another form of anaplastic carcinoma. × 388

adenoma so that blood-borne metastatic growths may develop at any time. Permeation of veins and local thrombus formation as well as tumor emboli are fairly common. The malignant adenomas thus differ sharply from the papillary lesions with respect to metastasis. With the former, the lymphatics become involved late, if at all, and lymphatic spread is unusual; with the latter, the lymphatics are involved early and there is consequently frequent lymphatic spread, while blood-borne metastatic growths are far more unusual.

Anaplastic Adenocarcinoma

All other types of adenocarcinoma of the thyroid, from the standpoint of biologic behavior, can be considered in one category. They are anaplastic, rapidly growing lesions of great histologic and cytologic diversity (fig. 8). The follicular pattern is usually completely lost. The anaplastic cells may be round, spindle shaped, small or large, and giant cells are common. Lesions made up of small round cells may resemble lymphosarcomas, whereas those composed chiefly of spindle cells suggest fibrosarcomas. In the more recent Mayo Clinic series, as reported by Pemberton and Black,[5] less than 20 per cent of carcinomas of the thyroid were of this type. Anaplastic adenocarcinomas may develop in a pre-existing goiter or within a nongoitrous thyroid. They infiltrate the capsule of the thyroid early to involve surrounding structures and metastasize by both lymphatics and blood stream. The acute, fulminating carcinomas of the thyroid are of this type. Usually their course is rapid, but occasionally, they progress far less rapidly than would have been predicted from their histologic structure. Almost invariably, regardless of treatment, by the time spread has occurred beyond the capsule of the thyroid, the ultimate outlook is hopeless.

Epithelioma

Approximately 1 per cent of the neoplastic lesions of the thyroid are squamous cell epitheliomas. Their origin is obscure, but they probably arise from small nests of squamous-cell epithelium occasionally seen in thyroid tissue. Although experience with such lesions is very limited, without exception they have been found inoperable or have proved incurable.

Sarcoma

There is still some disagreement concerning the question of sarcoma of the thyroid. Ewing and probably the majority of pathologists con-

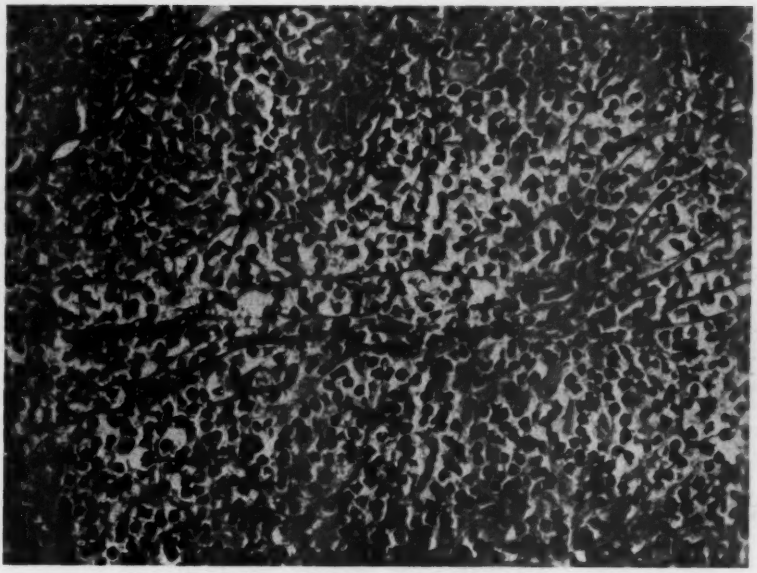

FIG. 8. Undifferentiated small-cell carcinoma. × 388

sider sarcoma quite rare. Others, including Wegelin and Graham, regard many of the extremely anaplastic lesions as sarcomas. The response to irradiation of certain of the small round-cell malignant lesions suggests that they should be classified with the lymphosarcomas rather than with the anaplastic adenocarcinomas. They are virtually always rapidly fatal except for the unusual lesion that responds to irradiation as do the lymphosarcomas.

TREATMENT

The treatment of cancer of the thyroid is primarily surgical. Irradiation is of secondary importance, being used for the most part, in cases in which not all malignant tissue can be resected. The extent of the operative procedure is governed by the type and extent of the local spread of the carcinoma. The conception of radical removal of the primary lesion along with the tributary lymphatics *en masse* is not particularly applicable to lesions of the thyroid because of the anatomical relationship of the thyroid to neighboring vital structures. Furthermore, there is much evidence indicating that radical dissections in the case of certain types of lesions are needless, whereas, in the case of other types of lesion, such dissections are useless.

Operability

In practically all cases, the lesion should be explored surgically. The only exception to this generalization would be the unusual case in which the lesion is so hopelessly extensive and fixed that it can neither be resected nor the trachea freed sufficiently to permit tracheostomy. With less extensive lesions, even after distant metastatic growths have developed, as much as possible of the primary carcinoma should be removed in an effort to preserve the airway and to prevent or relieve compression of the esophagus. Fixation of the thyroid does not necessarily indicate inoperability, since the fixation may not be due to malignant infiltration. As will be discussed subsequently, when treatment with radioiodine is considered, there are other important reasons for removing surgically as much of the carcinoma as possible, as well as uninvolved thyroid tissue in all cases considered suitable for treatment with this agent.

As a rule, papillary adenocarcinoma is present in only one lobe, but not infrequently the lesion may be bilateral. Also involved cervical lymph nodes may be discovered on either side of the

neck even if the mother growth is unilateral. It has been our policy, therefore, after determining the histologic characteristics of the tumor by frozen section, to perform a double partial lobectomy, leaving a very small portion of the thyroid remaining in the tracheoesophageal angle. The deep cervical lymph nodes are then removed from under the internal jugular vein throughout its entire length by simply retracting the vein laterally. As long as the tumor has not invaded the thyroid gland by spreading through the tumor capsule, it is unnecessary to perform a radical neck dissection. However, if the tumor has involved the strap muscles and contiguous tissue, a complete neck dissection should be performed. Any current controversy has to do largely with the extent of the dissection of the lateral cervical regions when involved nodes are present. Complete lateral cervical dissection, removing all nodes from clavicle to mastoid with sacrifice of the sternocleidomastoid muscle, strap muscles and internal jugular vein in all cases, is advised by some. Others believe that a more limited dissection, removing only the group of nodes in which spread has occurred and saving the sternocleidomastoid and internal jugular vein, is adequate. The necessary exposure is secured by extending the thyroidectomy incision cephalad along the posterior border of the sternocleidomastoid muscle. Occasionally, a second incision made paralleling a skin fold over the upper deep jugular nodes is advisable. I have long believed that limited dissections are as effective in controlling the disease as are block dissections, and the cosmetic result is far more pleasing. On the other hand, in cases with involvement of many nodes, particularly in older patients in whom the cosmetic result is of less importance, there can be few objections to block dissections. An adequate number of patients have been treated in each way to indicate that the ultimate results are comparable. Limited removal of individual, involved nodes through inadequate small incisions is to be strongly condemned because subsequent more adequate dissections are made far less satisfactory by the resulting scarring. Patients in whom a papillary adenocarcinoma has been removed should be examined at least every 6 months following operation, due to the fact that recurrence in the lymphatic glands may occur years later because of the slow growth of these tumors. Very minute collections of lymphatic tissue not visible at operation may develop in later years into palpable lymph glands. Because of the removal of so much thyroid gland and also to inhibit the pituitary gland secretion of thyrotropic hormone, it is well to administer thyroid extract to these patients after operation. As shown by the author in 1940 *Archives of Surgery*, when thyroid extract is given to a patient, orally, an atrophy of the thyroid gland is produced. The same effect is obtained in the tumor nodules if the follicles of the tumor contains colloid. However, diminution in size of the nodule should not mislead one into the belief that the papillary adenocarcinoma has receded or changed the character of its epithelial overgrowth. It has merely become less prominent and obvious.

Adenocarcinoma in an adenoma. The malignant adenomas are usually not locally invasive. They tend, however, to invade blood vessels so that bloodborne metastatic growths are characteristic. The appearance of a distant metastatic growth is occasionally the first clear evidence of the presence of carcinoma. Since the tumor has no lymphatics, metastasis to regional lymph nodes cannot occur until the capsule of the tumor has been infiltrated, a late event in the course of the lesion. As with the papillary lesions, the involved lobe should be excised totally through the usual incision used for routine thyroidectomy. The operative field should be carefully inspected for gross evidence of venous spread. If any of the thyroid veins are thrombosed, the thrombosed vein should be resected in continuity with the involved lobe. In advanced cases, this may necessitate resection of the superior and middle thyroid veins along with the segment of deep jugular vein delineated by the two sets of thyroid veins. Care should be taken not to dislodge the clots from the thrombosed veins. With this in mind, the jugular vein may well be ligated above the superior thyroid vein before the resection is begun. The resection of veins not thrombosed grossly is less rational.

In spite of the fact that there can be little objection to the removal of obviously involved cervical lymph nodes, there is little place in the treatment of the malignant adenomas for the routine prophylactic removal of the cervical lymph nodes or for extensive cervical dissections when involved nodes are found. By the time the

cervical nodes become involved, which is a late and somewhat unusual event, blood-borne metastatic growths will almost certainly have developed or the primary lesion will have become inoperable locally.

Anaplastic adenocarcinoma. Treatment of all anaplastic lesions of the thyroid is most disappointing. In spite of all therapeutic efforts of any type, by the time such lesions have spread beyond the thyroid, they are almost without exception incurable. They tend to grow rapidly, to metastasize early by way of both the lymphatics and the blood stream, and to infiltrate beyond the thyroid before the diagnosis is made. Every effort should be made to remove the primary lesion, if only to prevent obstruction to the trachea. However, the risk of radical resections of anaplastic carcinomas that have spread beyond the thyroid is not warranted, since the chance of cure is practically nil.

Epithelioma and sarcoma. Cumulative experience with such lesions is so limited that little can be said concerning treatment. Treatment, in my experience, has been unsatisfactory in every case in that all patients died of their disease, usually within a short time after treatment. Most fortunately, lesions of these types are rare.

Palliative Resection

Palliative surgical treatment has a most important place in the treatment of carcinoma of the thyroid. It is usually impossible to determine resectability, except in the most advanced cases, before surgical exploration. If the lesion proves inoperable locally, as much as possible of the malignant tissue should be resected. Similarly, subsequent external irradiation is more effective after resection of a large portion of the malignant tissue, since the treatment can be limited to smaller areas. In more advanced cases, the surgical procedure may have to be limited to biopsy and the provision of an airway. An extended effort to free the trachea from the carcinomatous mass is warranted in all cases in which surgical exploration is attempted. The restoration and maintenance of the airway are, in fact, among the principal aims of the palliative procedure.

Tracheostomy should be strongly considered in any case in which an extensive dissection is carried out in the immediate vicinity of the larynx and trachea. The indications for the procedure are even more definite when large masses of malignant tissue must be left behind or when irradiation is contemplated. As a rule, establishing the tracheostomy at the time of the original palliative procedure not only adds greatly to the safety of the procedure, but also is technically easy. In marked contrast, the attempt to find and open the trachea in the presence of tracheal obstruction owing to recurrent carcinoma is both extremely dangerous and technically difficult. I have, occasionally, in such neglected cases, introduced a bronchoscope to maintain the airways during the trying dissection necessary to find the distorted and displaced trachea.

The question of gastrostomy is occasionally raised in advanced cases with obstruction of the esophagus. In my opinion, the procedure is rarely if ever indicated.

External irradiation. Considering the extensive experience with external irradiation in the treatment of carcinoma of the thyroid, it is surprising to find so little agreement in the literature as to its effectiveness. It was formerly so relied upon that postoperative irradiation, at least, was advised in the great majority of cases. Whereas irradiation was thought far inferior to surgical resection as definitive treatment, it was considered of definite importance in destroying any small deposits that might remain after resection. Evidence of a statistical nature is available indicating that survival rates are somewhat better after resection followed by irradiation, than after resection alone. The majority of radiologists were convinced formerly, that irradiation not only decreased the rate of growth of practically all types of carcinoma of the thyroid, but actually led to a diminution in the size of the lesions.

There is less certainty at present as to the value of irradiation. Objective evidence that the less anaplastic lesions can be particularly influenced is largely lacking. There can be little doubt that the more anaplastic growths will occasionally regress after treatment. The improvement is usually temporary, and of limited benefit, even palliatively. In many institutions at present, irradiation is not carried out postoperatively in those cases in which all known carcinomatous tissue has been removed. The current trend is undoubtedly toward this prac-

tice, although combined therapy is still employed widely.

In all cases in which the primary lesion cannot be removed completely, external irradiation is usually advisable. The results of treatment in the case of papillary lesions and of malignant adenomas are difficult to evaluate. Measurable decrease in the size of the malignant mass usually does not occur. The response to treatment of an occasional anaplastic lesion may be temporarily quite striking. This is particularly true of lesions that resemble lymphosarcomas histologically. Certainly, all such lesions should be treated by a combination of resection and irradiation. Conversely, anaplastic lesions characterized by larger cells, including those resembling fibrosarcomas histologically and giant-cell-carcinomas, are little affected by external irradiation.

Interstitial irradiation. This form of irradiation, using radium needles or radon seeds, to treat small masses of unresectable carcinoma is more rational and probably should be more widely used. It is questionable whether any carcinoma of the thyroid has ever been cured by means of external or interstitial irradiation. Prolonged survivals after treatment can be attributed more reasonably to the inherent slow progression of the lesion. Irradiation of metastatic lesions away from the immediate vicinity of the thyroid is largely useless except for the control of pain.

Radioactive iodine. Radioactive iodine has a limited, although definite, place in treatment in selected cases of inoperable carcinoma of the thyroid. It has no place in the treatment of resectable lesions, which, of course, should be removed surgically, if this is technically possible. The treatment is complex, time consuming, uncertain with regard to ultimate results, and not without danger. It should, consequently, not be undertaken lightly or by anyone not thoroughly familiar with the problems. The following brief description of the method has been included only to illustrate these points.

Inoperable extensions or metastatic growths can be treated effectively only if the malignant tissue can be stimulated to concentrate sufficient radioactive iodine. Rarely, a malignant lesion will concentrate iodine even in the presence of the thyroid. Far more commonly, this function must be stimulated before treatment is possible, and in any case the thyroid gland must be removed totally or destroyed by means of radioactive iodine before the malignant tissue can be treated.

Certain types of lesions cannot be treated with radioactive iodine because they cannot be stimulated to concentrate the isotope. All anaplastic lesions, without exception, are of this type. The Hurthle-cell type of malignant adenoma and papillary lesions with no follicular component, the so-called pure papillary adenocarcinomas, can be stimulated to trap iodine so rarely that an attempt to treat lesions of these types with radioactive iodine is practically always destined to fail. Similarly, malignant adenomas characterized histologically by solid sheets of cells without follicles or colloid formation are a most unfavorable group. Conversely, with all other types of carcinoma of thyroidal origin, the possibility of being able to affect the lesion by isotopic irradiation is sufficiently good to warrant making the attempt. There is a definite correlation between the presence of follicles, particularly with follicular formation and colloid, and the function of concentrating iodine. The probability or improbability that the lesion can be treated can thus be judged from the histologic structure of the lesion with fair confidence.

The first step leading to ultimate treatment is the demonstration by surgical exploration of the thyroid that the lesion is in fact not resectable or, in the case of a lesion with distant metastatic growths, that the carcinoma actually arose in the thyroid. As previously discussed, as much of the malignant tissue as possible is resected. If the lesion is of the type, as just discussed, in which there is a reasonable possibility of stimulating uptake, total thyroidectomy is carried out. If the lesion is inoperable because of local extension, it is still often possible to remove practically all, if not all, of the uninvolved thyroid. In any case, as much as possible of the thyroid is removed. In those cases, in which the thyroid cannot be excised surgically, the gland must be destroyed by radioactive iodine. Surgical ablation is much superior to destruction with radioactive iodine for reasons that are still not entirely clear.

The patient is then given an antithyroid drug, which does not contain iodine, for several months, usually for at least 3 months. The therapeutic aim should be the production of complete myxedema. This provokes the secretion of thyroid-stimulating hormone, which pre-

sumably acts to stimulate the iodine-trapping function of the lesion to be treated. Ultimately, administration of the antithyroid drug is discontinued, and 48 hours later the iodine-concentrating function of the lesion is determined by means of a tracer dose of radioactive iodine. If the uptake is adequate, as judged by *in vivo* counting and by studies of urinary excretion, a massive dose of radioactive iodine is given. The same program is then repeated until there is no longer any uptake or until the patient has received the maximal permissible dose of radioactive iodine.

Many of the quantitative aspects of the treatment are still unsettled, and the dosimetry of both external and internal irradiation is beyond the scope of the present presentation. If an adequate uptake cannot be stimulated by total thyroidectomy and antithyroid drugs for 6 months, it is improbable that the lesion can ever be stimulated to concentrate iodine. It is probably advisable to withhold external irradiation until all hope of being able to treat with radioactive iodine has been abandoned.

The ultimate results of treatment cannot as yet be evaluated. In many cases, metastatic growths apparently have been destroyed. Prolonged survival without evidence of disease has been achieved in others. Treatment has failed in many cases because of the development of metastatic growths that cannot be made to concentrate iodine. At the present time, an attempt to stimulate uptake should undoubtedly be made in all cases in which the lesion is inoperable and is of one of the types capable of concentrating iodine.

PROGNOSIS

Prognosis is largely dependent on the type and extent of the lesion. The ultimate outlook after treatment differs so greatly with lesions of different types that the several types should not be grouped together when considering either prognosis or treatment. In the case of the less anaplastic lesions, survival rates are not a particularly adequate measure of success of treatment because of the slow natural course of these lesions. It cannot be assumed that a patient living and presumably well some years after treatment is, in fact, cured nor that the prolonged survival resulted from the treatment. The difficulties in attempting to evaluate different methods of treatment in terms of survival rates are most evident.

Papillary adenocarcinoma. In cases in which all of the lesion can be removed, the survival rate does not differ greatly from that of the general population when corrected for age. Local recurrence is not particularly common nor is the appearance of distant metastatic growths after removal of the primary lesion. Metastatic lesions not infrequently become evident in regional lymph nodes even years after removal of the primary. As previously discussed, such involved lymph nodes do not become fixed to surrounding tissues so that, practically without exception, they can be removed. The late development of enlarged cervical lymph nodes definitely does not indicate that the lesion has become inoperable.

If the primary lesion has infiltrated beyond the capsule of the thyroid, the prognosis must be more guarded. Unlike the metastatic deposits in lymph nodes, the primary lesion is infiltrative and ultimately involves surrounding tissues. In cases of this type late recurrences and distant metastatic lesions may, of course, occur and lead to the death of the patient. In terms of survival rates, well over 90 per cent of patients may be expected to survive for 5 or more years and more than 80 per cent for 10 or more years.

Survival rates are far less satisfactory among cases in which the lesion cannot be removed completely, either because of local extension or because of distant metastatic lesions. In spite of palliative treatment, approximately one-third of patients fail to survive for 5 years, and two-thirds will have died by the end of 10 years. The prolonged survival rates among patients with unresectable lesions are probably more attributable to the slow course of such lesions than to treatment. Distant metastatic growths, and particularly pulmonary metastatic lesions, are not incompatible with prolonged survival without symptoms. Death usually results from complications incident to local recurrence, emphasizing again the extreme importance of (1) surgical exploration even after distant metastatic growths have appeared and (2) removal of as much of the primary lesion as possible.

Adenocarcinoma in an adenoma (malignant adenoma). Survival rates are definitely less satisfactory in malignant adenomas than those after treatment of papillary lesions. Local

recurrence is fairly common, and distant metastatic growths tend to be multiple and to progress with moderate rapidity. In marked contrast to papillary lesions, the presence of involved cervical lymph nodes is an ominous finding, since local lymphatic spread is usually preceded by distant hematogenous dissemination. Death results from local recurrence or distant metastatic growths or both. Among cases in which the lesion is resectable, the 5-year survival rate is approximately 70 per cent and that after 10 years is somewhat higher than 50 per cent.

In the past, palliative treatment was most unsatisfactory. Survival beyond 5 years was fairly common, while that beyond 10 years was unusual. This discouraging outlook may be definitely changed by the advent of radioactive iodine. If the lesion has a follicular component, it can usually be stimulated to concentrate sufficient radioactive iodine to permit treatment with this agent. The late results after internal irradiation cannot as yet be judged, but at least a method of some promise for treating such inoperable lesions has been developed.

Anaplastic adenocarcinoma. The results after treatment of anaplastic adenocarcinomas are most unsatisfactory. Whether resectable or not, and regardless of the type of treatment, the outlook is decidedly poor. Less than 10 per cent of patients survive for 5 years, and less than 5 per cent survive for 10 years. The response of lesions characterized by small round cells resembling lymphocytes to external irradiation may be initially quite striking. Ultimately, however, the treatment usually proves ineffective. It is fortunate that less than 20 per cent of all carcinomas of thyroid origin are of this type, since, for practical purposes, no effective treatment is available.

Nodular goiter without hyperthyroidism. Nodular goiter without hyperthyroidism associated with various cardiac arrhythmias, such as auricular fibrillation, premature systoles, or paroxysmal tachycardia, has been somewhat forgotten because of the many discussions of its relation to carcinoma of the thyroid. However, in spite of the lack of clinical or laboratory evidence of hyperthyroidism, this type of adenomatous goiter has an insidious toxic effect with special emphasis upon the cardiovascular system. In the past, this type of disease of the thyroid has been designated by the indefinite terms, such as toxic adenoma, hyperfunctioning adenomatous goiter or dythyroidism. The calorigenic manifestations of Graves' disease are absent, *i.e.*, protein-bound iodine (PBI) and basal metabolic rate (BMR) are normal. Some other substance secreted by the thyroid gland other than thyroxine may probably be responsible for these toxic effects. Arrhythmias of not more than one year's duration will, as a rule, revert to a normal rhythm in a few days or weeks after thyroidectomy. In those instances in which the arrythmia persists after operation, the patient can be maintained on a small dose of digitalis. Antithyroid drugs have no place in the treatment of toxic goiter with cardiac arrythmia; the condition is far too urgent. They definitely play no part in the preoperative preparation of such patients. Total thyroidectomy is a misnomer but total thyroidectomy expresses the fact that fragments of thyroid tissue were left behind in the neighborhood of the recurrent laryngeal nerve and the parathyroid glands. As a consequence, there accrues as a result of the operation, a physiologic ablation of the thyroid gland which may lead to a spontaneous return to a normal rhythm.

INFLAMMATORY LESIONS OF THE THYROID

Acute Thyroiditis

Inflammatory surgical affections of the thyroid gland that are unequivocally due to invasion of the parenchyma of the thyroid via the blood stream by pyogenic organisms are quite rare, but do occur. As a rule, such inflammatory lesions are localized to one lobe and, for some reason or other, most frequently on the right side.

The signs and symptoms of such a localized abscess differ in no way from such an affection in any other organ or part of the body. The symptoms are usually pain on swallowing, tenderness, with an elevation of temperature from normal to 100 or 101° and eventually, redness of the skin over the area. The treatment for this type of infection is like that for other similar abscesses, namely incision and drainage.

Histologically, the thyroid gland in these cases shows a marked infiltration around the site of infection of polymorphonuclear leukocytes and small lymphocytes—also destruction of follicles with compression of adjacent ones, which give the appearance of a false capsule. Similarly,

but very rarely, one may encounter a localized tubercular abscess with caseation which on histologic examination shows typical formation of tubercles with surrounding epitheloid cells and tuberculous giant cells with their peripheral distribution of the nuclei. Not infrequently tubercle bacilli can be cultured from tissue removed at biopsy.

The treatment for such a lesion, in addition to the antibiotic drugs, namely *p*-aminosalicylic acid and streptomycin, would be lobectomy, removing with a wide margin the entire lesion. Not infrequently in the past a mistake in diagnosis of tuberculous thyroiditis has been made due to the fact that during involuting processes in the thyroid gland, colloid escaping through the burned out or ruptured follicles into the interstitial tissue produces a foreign body reaction, which attracts giant cells to the locality of the escaped colloid. However, these giant cells do not have the typical peripheral nuclear distribution, but on the contrary, the nuclei are centrally placed.

Subacute Thyroiditis

This inflammatory process in the thyroid gland comes on insiduously, with a slow but gradual enlargement of usually the right lobe followed by the isthmus and extending over and including the left lobe of the thyroid gland. As in an acute thyroiditis the first signs and symptoms are enlargement of the gland with pain on swallowing, accompanied by tenderness, with an elevation of temperature in the first week running up to 101 and 102°. After about 1 to 2 weeks, the entire thyroid gland is enlarged, brawny, and definitely increased in consistence. It can be differentiated clinically, however, from other cases of diffuse enlargement of the gland by the fact that it comes on rather acutely and has a definite febrile reaction. The white blood count is not elevated, as a rule, and the disease will subside spontaneously, with the gland returning to its normal size and consistence in a period of 3 weeks to 6 months. Biopsies of the gland in the acute stage have revealed a marked lymphocytic infiltration, but very little, if any, polymorphonuclear leukocytes.

The treatment for this condition is nonsurgical, but since the advent of cortisone, there have been some reports in the literature that this condition has responded rather promptly to the administration of cortisone. X-ray radiation therapy is definitely contraindicated.

Hashimoto's Struma

This is a questionable inflammatory process, but undoubtedly it is due to marked lymphocytic infiltration of the thyroid parenchyma and involves both lobes. The thyroid greatly enlarges and becomes very markedly increased in consistence. The enlargement is diffuse, and the patient becomes aware of a sense of pressure on the trachea and a sense of difficulty in breathing in the recumbent posture. The enlargement of the thyroid then is discovered, and the question again arises as to whether or not the enlargement is due to a malignant change.

The basal metabolic rate and the radioactive iodine uptake in these cases are usually normal, or possibly subnormal. On account of the difficulty in differential diagnosis, this affection of the thyroid gland should be operated upon. At the operating table a rubberlike consistency of the thyroid gland which is far greater than the normal thyroid consistency, and also the enlargement of the gland, are immediately noted. The circulation in these glands is very much reduced and there is also an absence of any enlarged lymph glands in the deep cervical chain. In cutting across the lobe a slight yellowish color to the parenchyma, sometimes varying from white to a lemon yellow will, to the experienced eye, reveal the identity of the lesion, which can be confirmed also by frozen section. The problem in these patients is to decompress the trachea, leaving as much of the right and left lobes as possible, for otherwise postoperative clinical hypothyroidism or even myxedema may occur. It is a mistake to do more than take out the isthmus of the gland, for when an isthmectomy is done the lateral lobes have no point of purchase. Thus, their power of compression is eliminated. It is incorrect, however, to do a radical double partial lobectomy, because it is totally unnecessary.

Riedel's Struma

Both lobes and the isthmus of the thyroid in this condition are diffusely involved and the gland stony hard in consistency. The patient, as in Hashimoto's struma, usually is aware of an enlargement of the thyroid gland and pressing on the trachea; however, the enlargement of the

thyroid gland may be minimal, but due to the fact that there is always some clinical doubt as to the exact nature of the lesion, an exploratory operation should be performed. A biopsy is taken and sections show a marked fibrosis not infrequently associated with solitary areas of calcification. In one patient, which was the first one ever operated on at The Johns Hopkins Hospital, I was forced to use rongeurs to remove the isthmus. The true nature of this affection can be immediately determined at the operating table by the appearance of the gland, which is usually white, anemic, and very difficult to cut with a scalpel. The thyroid parenchyma, due to this scarring, is very much reduced and therefore the radioiodine uptake and the basal metabolic rates are subnormal. An examination along the internal jugular veins reveals no enlargement or involvement of the deep cervical lymph glands. Whether or not this condition is a continuance of a chronic inflammatory process, of which Hashimoto's struma is a precursor, is controversial. Patients who have died of other conditions unrelated to the thyroid gland that have been operated on for Hashimoto's struma some years previously, show no change in the histologic structure of the gland. There is not one bit of evidence to prove that one condition merges into the other, but the therapeutic endeavor is absolutely the same in both. In other words, in Riedel's struma as in Hashimoto's struma, only the isthmus should be removed and for the same reason. If in Riedel's struma the gland is allowed to remain *in situ*, the pressure on the gland will become so great that eventually a tracheostomy will have to be performed. It is essential that an isthmectomy be done and that the trachea be completely decompressed. The remaining lobes of the thyroid gland should be left *in situ* to provide sufficient thyroid function to prevent the patient from becoming hypothyroid.

Diffuse Colloid Goiter

Patients with an enlarged diffuse colloid goiter, which is usually asymptomatic except for an unsightly bulge or enlargement of the gland in the neck and minimal evidence of hypothyroidism, often present themselves for operation. This is particularly true in preadolescent girls who, at that age, sometimes are quite sensitive about an enlargement in the neck.

These patients should not be operated upon for cosmetic reasons. This condition is listed amond the aforementioned surgical affections of the thyroid gland merely to warn of the undesirable effects of removing a portion of each lobe to counteract the swelling in the neck. An atrophy of this type of gland can be obtained by oral administration of thyroid extract, with dosage to be determined by trial, and increased or decreased according to the rapidity of the subsidence of the thyroid gland. Double partial lobectomy of the thyroid gland only further embarrasses the already underproduction of the secretions of the thyroid gland.

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REFERENCES

1. Asper, S. P., Jr.: Observations on the preparation of hyperthyroid patients for the subtotal thyroidectomy with propylthiouracal. Surgery, *34:* 655, 1953.
2. Cole, W. H., Slaughter, D. P., and Majarakio, J. D.: Carcinoma of thyroid gland. Surg. Gynec. & Obst., *89:* 349, 1949.
3. Cope: Personal communication.
4. Lahey, F. H., and Ficarra, B. J.: The lateral aberrant thyroid. Surg. Gynec. & Obst., *82:* 705, 1946.
5. Pemberton, de J., and Black, B. M.: *Cancer of the Thyroid.* American Cancer Society Monograph, 1954.

HEMIPELVECTOMY AFTER 68 YEARS*

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When, in 1891, Billroth performed a hemipelvectomy, the patient succumbing within a few hours, this Titan of the early days of operative surgery failed even to report the experience. Fortunately, Savariaud[15] in 1902, reporting his own unsuccessful attempt, made mention of Billroth's experience. Savariaud stated that Girard of Berne learned from Berg of Stockholm, who was visiting his operating room, that Berg had assisted Billroth in the first completed hemipelvectomy. Girard in 1895[4] had performed the first hemipelvectomy, with survival of the patient, and in 1898 another.[5] Savariaud found reports of 13 cases in all, one of them that of Salistcheff of Tomsk, in Russia, in 1900. Nine of these patients had died because of the operation.

In this country there are two reports of early performance of this operation, with fatal outcome, by Ransohoff[13] in 1909, and by Keen and Da Costa[3] in 1904. No further reports appeared until the 1942 reports of Leighton[12] and of Morton.[11] This lack of interest in the operation for so long in this country is remarkable. It was already widely practiced all over Europe, although the mortality was formidable. Today there are a number of individual experiences of 30 to 50 such operations,[3, 6, 12, 16] and Sir Gordon Gordon-Taylor[6] has performed the hindquarter amputation "102 times, twice since I have become an octogenarian." Gordon-Taylor's mortality, 50 per cent in his earlier experience, has steadily declined.

In our experience,[2, 14] and that of others,[1] the risk of fatal outcome appears to be small. The old fear that this is an "intrinsically shocking procedure" has been dispelled. With deliberate and precise operating, blood loss is readily controlled and replaced, and the operative hazard found to be small. In our series of 28 such operations, in patients ranging in age from 13 days to 70 years, we have had only 2 deaths. One was in a woman with a gratifyingly smooth immediate postoperative course, who was on crutches the day after operation, and left the hospital on the 22nd day to drive directly to Florida. Two months later she suddenly became ill, deeply jaundiced, and died after 4 days—surely a homologous serum hepatitis. The other was a massively obese woman of 63 years who developed auricular fibrillation the day after operation, and died abruptly while being bathed, 18 days after operation. Autopsy revealed a heart extensively infiltrated with fat.

A large segment of the medical profession remains to be convinced that the operation is not excessively deforming and mutilating, and that its results are worth while. A brief review of our experience will indicate that, with a low mortality rate and short hospital stay, patients with grave, and otherwise lethal malignant lesions of the bone or soft tissues of the pelvis or upper thigh, may, in some instances, remain well indefinitely, and in others are relieved of painful or ulcerated and unbearable tumors to live out their lives in relative comfort.

The most generally accepted indication for hemipelvectomy is the chondrosarcoma of the pelvis or upper femur. We have had only three such cases, one was in a patient who had had one local operation for chondrosarcoma, involving the sacroiliac joint, and causing great pain. For 5 years after hemipelvectomy she wore a prosthesis, drove a car, did her own housework and was free of pain. A lobectomy for pulmonary metastasis prolonged her life for another year. The 2nd patient, a woman of 43 years, is alive and well 8 years after operation and has a prosthesis, but does not use it regularly. The 3rd patient was a 70-year-old man with a huge tumor causing great pain and narcotic addiction. He obtained great relief from operation. Osteogenic sarcomas are thought by some to be too malignant to justify this operation, but we have 2 patients, alive and well, after 9 years and 7 years respectively, in our group of 10.

Our poorest results have been in the soft tissue

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sarcomas of which we have had 6, with only 1 survival much more than a year beyond operation. That patient is a boy, now 7 years old, 3 years after hemipelvectomy for a recurrent fibrosarcoma deep in the buttock. Most of these patients with malignant soft tissue tumors had had repeated local "extirpations," with repeated recurrence, and deaths were from distant metastases. If a properly radical local operation is prohibited by the location of a malignant connective tissue tumor in the pelvis or groin, a life may be saved by performing hemipelvectomy early, as an elective procedure, rather than late, as a measure of desperation.

The operation was performed twice for melanosarcoma, 1 patient is alive, with recurrence after 2 years, the 2nd is a woman who had extensive local recurrences in a midthigh amputation stump, in the skin of the thigh, and in the iliac glands, after amputation for recurrent melanosarcoma in the leg. This patient is alive and well 10 years after her hemipelvectomy.

Epithelial malignancies metastasizing to the groin may produce huge fungating ulcers, causing great pain, unbearable stench, and the constant danger of massive hemorrhage. Indeed 1 hemipelvectomy[3] has been performed as an emergency for such massive femoral hemorrhage. In such patients the operation is complicated technically by the necessity for resecting the inguinal ligament and skin of the right lower quadrant. Nevertheless the operation was completed successfully in all of the 5 patients operated upon for epithelial malignancies of the groin, or hip, and the wounds closed without the need for grafts. In all, the immediate result was gratifying from the standpoint of relief of pain, disappearance of odor and healing of the wound. Four patients survived, relieved of their symptoms, 2 years, 1 year, 1 year, and 6 months, and the 5th is living and well 13 years after hemipelvectomy for a squamous cell carcinoma of the buttock, extending into the pelvis through the sciatic notch.

We feel, then, that the indications for the hindquarter amputation are:

1. Malignant bone and cartilage tumors of pelvis or upper femur.

2. Malignant soft tissue tumors of thigh or pelvis not anatomically susceptible to a radical *en bloc* dissection with wide margins on all sides.

3. Occasional instances of late and neglected osteomyelitis and pyarthrosis (we have one such in a patient with an operatively fused knee who developed a secondarily infected tuberculosis of the hip on the same side, with multiple draining sinuses).

4. Fungating metastatic malignancies of the groin, not susceptible to a local operation. The operation here is frankly palliative, but a year or two of comfortable life, and immediate relief from the pain and stench of the lesion, have seemed well worth the operation and the 10 to 21 days of hospitalization.

5. In one instance the operation was performed in a 13-day-old infant for a massive mixed angioma obscuring the limb in its depths and already ulcerated. The tumor extended from the pelvis to the toes. The child is well and happy 13 years after operation.

Some of the lesions listed above, particularly the sarcomas of the upper femur, could have been considered suitable for treatment by hip joint disarticulation. We made the point in 1950[14] that the hip joint disarticulation is technically more difficult, involving, as it does, transection of great masses of muscle, and that it is much less satisfactory as an operation for malignant lesions, since it provides a much narrower margin and transects nerves and muscle planes which are invaded by tumor at a lower level. After both amputations a prosthesis can be made, although the prosthesis is often found to be so bulky that the patient will not wear it. On the other hand, some of our patients wear prostheses without the use of cane or crutch. It is true that patients, with a hip joint disarticulation, do have 2 ischial tuberosities and find sitting simpler. However, the difficulty in sitting down is a temporary one, after hemipelvectomy, and after 3 to 4 months patients are no longer conscious of this as a problem.

Sexual function in these patients is not interfered with by the operation, and at least one woman is reported to have delivered after a hemipelvectomy. Urinary function and rectal function are affected only in the immediate postoperative period.

Although the operative site bulges when the patient coughs, we have seen no true hernia, even in the 9- and 10-year survivals. One patient had a nylon mesh put in by another surgeon because of the bulge in the stump. Infection

resulted, and the mesh was removed. The wound, 5 years later, shows no hernial protrusion.

TECHNIQUE OF OPERATION

The position of the patient on the table is most important. The patient should be supported by a roll under the shoulder blades, and another under the opposite hip. A catheter is placed in the bladder. The extremity is draped, the field including the buttock almost to the anus, the border of the scrotum or vulva, the abdomen to beyond the midline, the back to the midline, and the costal margin.

A curved incision from the anterior superior spine to the pubis is carried down through the fat, and the deep epigastric vessels divided.

The inguinal ligament is detached from its medial and lateral bony attachments. Medially the rectus and pyramidalis are separated from the pubis and laterally the abdominal muscles and latissimus from the anterior superior spine. The peritoneum is stripped from the iliac fossa. One can see the femoral and iliac vessels and determine the extent of lymph nodal involvement. It is possible at this point to retreat without a penalty. In an instance of a neurosarcoma arising within the pelvis in a patient with von Recklinghausen's disease, we found at this stage that the area of fixation of the tumor crossed the sacrum. The amputation was abandoned and the inguinal ligament re-attached and the wound closed.

The common iliac vessels are ligated and divided high, almost at the aortic crotch, and the internal iliac doubly ligated and divided. Much has been written of jeopardy to the posterior flap resulting from common iliac division. It has been our experience that in spite of this division, the circulation of the posterior flap is good, and that bleeding from the gluteal vessels may be as vigorous as if no ligations had been performed, an indication of the efficacy of the normal collaterals.

The psoas muscle is divided with the cautery and the femoral nerve lying behind it ligated and divided. Phantom limb pain has not been a problem in our patients, and we have simply clamped and ligated the nerves as far proximally as possible.

The pubis is divided with scalpel or osteotome, through the symphysis. This is quite easy, and simpler than our former employment of a Gigli saw. The attempt to demonstrate completeness of division may cause retropubic bleeding, particularly in the male. This is merely controlled by a pad until the amputation has been completed and the area is accessible.

The skin incision is carried around posteriorly behind the greater trochanter to the crease of the thigh medially, and then up to the beginning of the incision on the pubis.

The skin flap on the buttock is laid back until the sacrum can be felt. The origin of the gluteus maximus is divided with the electrocautery revealing the piriformis muscle and sacrospinous and sacrotuberous ligaments. The superior and inferior gluteal vessels emerge above and below the piriformis and the sciatic nerve lies behind it. During the posterior dissection the knee and hip are strongly flexed and the hip adducted so that the patient is partially rolled over. The gluteal vessels are secured, the piriformis divided and the sciatic nerve clamped, divided and ligated.

The sacrospinous and sacrotuberous ligaments being divided, an instrument can be inserted through the sciatic notch to emerge above the posterior superior spine. A Gigli saw is pulled through at this point. Particularly if it is desired to remove all of the ilium, the quadratus lumborum is separated from the posterior portion of the iliac crest, so that the saw may pass behind the posterior superior spine. The bone is sawed through, the levator ani and ischiocavernosus muscles divided, and the specimen removed. Any bleeding points are now readily available. Bleeding in the spongy tissues around the vagina and urethra may require careful transfixion with fine silk. The bone is treated with wax if necessary. The inguinal ligament, posteriorly, is tacked to the sacrum, drains placed through the posterior flap, and the skin closed with subcutaneous and cutaneous sutures. The operation takes 1½ to 3½ hr. and requires 3 to 5 units of blood.

SUMMARY

Hemipelvectomy is now a well established operation indicated for malignant disease of the upper thigh or pelvic girdle. The operative mortality is low, the morbidity acceptable, survival depending upon the particular nature of the neoplasm. Long term survivals have been achieved in all groups; bone sarcoma, chondrosarcoma, fibrosarcoma, and carcinoma. In those

patients not cured, the amputation has prolonged life usefully, often for several years, relieved distressing symptoms and prevented the appearance of others.

We report 28 operations, with 2 deaths, 1 cardiac in a woman of 63 years, who died abruptly 18 days after operation, and 1 of homologous serum jaundice 2 months after operation.

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ADDENDUM

Since this paper was submitted, the group has been increased to 31 patients with no further operative deaths. The indications for the last 3 cases were 1 massive neurogenic sarcoma, 1 metastatic hypernephroma and 1 myxosarcoma.

REFERENCES

1. Beck, N. R., and Bickel, W. H.: Interinnomino-abdominal amputations. J. Bone & Joint Surg., *30-A:* 201, 1948.
2. Buchholz, R. R.: Interinnomino-abdominal amputation, a report of a case. Welborn Hospital Clinic Bulletin, *22*, 3, 1949.
3. Coley, B. L., and Higinbotham, N. L.: Management of malignant disease in the neighborhood of the hip. Surg. Gynec. & Obst. *99:* 727, 1954.
4. Girard, C.: Désarticulation de l'os iliaque pour sarcome. Rev. de Chir., *15:* 952, 1895.
5. Girard, C.: Sur la désarticulation interilio-abdominale. Rev. de Chir., *18:* 1141, 1898.
6. Gordon-Taylor, G.: Personal communication, 1958.
7. Gordon-Taylor, G., Wiles, P., Patey, D. H., Warwick, W. T., and Monro, R. S.: The interinnomino-abdominal amputation. Observations on a series of fifty cases. J. Bone & Joint Surg., *34-B:* 14, 1952.
8. Hudson, O. C., and Janelli, D. E.: Emergency hemipelvectomy. Am. J. Surg., *88*: 340, 1954.
9. Keen, W. W., and DaCosta, J. C.: A case of inter-ilio abdominal amputation for sarcoma of the ilium and a synopsis of previously recorded cases. Internat. Clin., *4:* 127, 1904.
10. Leighton, W. F.: Interpelviabdominal amputation. Report of three cases. Arch. Surg., *45:* 913, 1942.
11. Morton, J. J.: Interinnomino-abdominal (hindquarter) amputation. Ann. Surg., *116*: 628, 1942.
12. Pack, G. T.: Major exarticulations for malignant neoplasms of the extremities. Interscapulothoracic amputation, hip-joint disarticulation, and interilioabdominal amputation. A report of the end results in 2[illegible] cases. J. Bone & Joint Surg., *38-A:* 249, 1956.
13. Ransohoff, J.: Inter-ilio abdominal amputation. With report of a case. Ann. Surg., *4*: 925, 1909.
14. Ravitch, M. M.: Hemipelvectomy. Surgery, *26:* 199, 1949.
15. Savariaud, M.: Un cas de désarticulation inter-ilio abdominale. Rev. de Chir., *26:* 345, 1902.
16. Taylor, G. W., and Rogers, W. P., Jr.: Hindquarter amputation. Experience with eighteen cases. New England J. Med., *249*: 963, 1953.